BRITISH HEART JOURNAL

Volume VIII
1946

LONDON
Reprinted by offset litho for
WM. DAWSON & SONS LTD
4 Duke Street, Manchester Square, London, W.1
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1958

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THOMAS LEWIS

Thomas Lewis was born at Cardiff on December 26, 1881. His father and mother, who were both Welsh, took a great interest in the education of their children and to this Lewis attributed his later success as a scientist. Except for one year at Clifton College, Lewis, up to the age of sixteen years, was educated entirely at home. He took little interest in book learning during these years, preferring to spend his time in the country, satisfying his innate curiosity in respect of natural objects, and his interest in outdoor sports. Before he was ten years old he had decided to become a doctor, but he apparently failed to realize the educational implications of this decision, for he failed in his London matriculation examination when he was sixteen. This failure, as one would expect, did not deter him, but goaded him to apply himself to his books.

A year later he matriculated in the first division in the University of London and never failed in any subsequent examination. A brilliant student career followed, first at Cardiff and later at University College Hospital, London. In 1905 he qualified as M.B., B.S. (London), winning a triple distinction and the University Gold Medal, and gained the D.Sc., Wales. During this time he had already shown his interest in research, for, with Swale Vincent at Cardiff, he had published a series of papers on the proteins of unstriped muscle and on the hæmolymph glands. As a student at University College Hospital he carried out some researches but stated that he achieved nothing. He was, however, meeting men of great ability such as Dale and Elliott and Noon of the Physiological Society, lunching with seniors like Starling, Bayliss, and Cushing, and it was quite clear that his interest was steadily moving in the direction of a research life.

He started work, in fact, in Starling's physiological laboratory in 1907; but in 1909 he put up his plate in Wimpole Street. This action, which suggested that he could not make up his mind whether to take up a research career or a consultant's life, was determined by the fact that opportunities for full-time research were practically non-existent to a man without private means. Lewis, though the son of a well-to-do father, was not the man to rely on parental wealth.

In 1908 Lewis met James Mackenzie. He was stirred by Mackenzie's critical attitude to medicine, and his independence of authority, under the spell of which he had fallen while in hospital. Mackenzie had a profound influence, for not only did he urge Lewis to take up research but suggested a problem, namely, the analysis of irregular cardiac actions. Lewis quickly saw that the string galvanometer, which Einthoven had recently developed, was the instrument most likely to give results in this field, and started his researches, both in the laboratory and the clinic, which added so much knowledge to the subject. Even at this stage his careful nature did not allow him completely to take the chances of a research life, so he combined hospital work and private practice with his research work. In 1910 he obtained the first of the newly created Beit Memorial Fellowships, but he did not relinquish private practice until 1916, when he was appointed a physician on the staff of the Medical Research Committee, as the Medical Research Council was then called.

He was then able to throw all his energies into research, as he had long wished to do. Even during the transitional period he achieved more than most would have done, had they given their full time to research. He published in 1911 his first book, *The Mechanism of the Heart Beat*, a book written for advanced students which gained in size as new knowledge, mainly from his own laboratory, was obtained, and became the " bible " of all those interested in cardiographic work. About the same time he also published two small books, namely *Clinical Disorders of the Heart Beat* (1912) and *Clinical Electrocardiography* (1913), which were written for practitioners. The character of these two books clearly indicates what Lewis always kept in mind: to seek for new knowledge and to use it for the simplification of diagnosis

and treatment of the sick. In addition, not satisfied with the opportunities for publishing the scientific data of his work, he founded in 1909 (with Mackenzie's help) and edited a new journal, *Heart*.

In 1916, when Lewis was only 33 years old, he published a series of remarkable papers in the Philosophical Transactions of the Royal Society; they detailed with remarkable clarity the spread of the electrical process across the chambers of the heart, when it was beating normally and abnormally, and related the findings to normal and abnormal human electrocardiograms. These papers are models of publication, not only in the clearness of presentation but also in the beauty of the illustrations, all of which he prepared himself. (Of this mass of work, that relating to the electrocardiogram of right and left bundle branch block has alone failed to stand the test of time.) This work was outlined in his Croonian Lecture to the Royal Society in 1917, and he was elected a Fellow in 1918.

During the First World War, Lewis was asked to investigate the condition known as " Soldier's heart " (D.A.H.) which was causing a serious loss of man power in the Army. With Meakins and Parkinson he directed the clinical services of a special hospital for this purpose, first at Hampstead and later at Colchester. With his characteristic energy he tackled his new problems and defined the condition, which he renamed " effort syndrome," and devised a treatment of graduated exercises which was eminently successful. As consulting physician to the Ministry of Pensions he took the opportunity of keeping in touch with a large number of soldiers pensioned with heart trouble for a sufficient length of time to gain further knowledge of the diagnosis, prognosis, and treatment of patients suffering from real or suspected cardiac disease. He also published a paper on dermatographism presenting the evidence for the independent contractile power of the capillaries. He received the C.B.E. in 1920 and a year later was knighted for his work during the war and for the Ministry of Pensions.

The war over, Lewis took up the study of the mechanism underlying auricular flutter and fibrillation. By a series of interrelated experiments on dogs and human beings, he concluded that the mechanism was that of a wave circulating around the mouths of the great veins. It was in his view a " circus movement " similar to that already described in cold-blooded contractile tissues. This conception has been generally accepted, though some workers could not unreservedly accept it.

When he was about 43 years old, the character of his researches underwent a striking change. He had decided that the proper subject to study was man, and henceforward he worked with man almost to the exclusion of animals. He gave up the complex technique of electrocardiography, involving animals, and turned to problems in man, using simpler techniques. He took up problems that had interested him during the war and studied the reaction of the skin vessels to injury. He obtained evidence that with all forms of injury a substance, "H substance," was liberated, which was indistinguishable from histamine, but which he refrained from calling histamine, as conclusive evidence was lacking. All this work he published in his book *Blood Vessels of the Human Skin*.

In 1927 he was awarded a Royal Medal by the Royal Society. In the same year work was interrupted by his first attack of coronary thrombosis; unacquainted with the recent American work on this subject he did not at first recognize the nature or the seriousness of his illness. It was with difficulty that he accepted the need for prolonged rest. The pain he suffered was intense, and this stimulated his later interest in this subject. He made an excellent recovery, but, recognizing the need for less strain he moved to the country, choosing gardening and fishing as recreations. He again set to work and continued his observations upon peripheral blood vessels, and showed that the pain of intermittent claudication was due to a chemical and physico-chemical stimulus which he called factor P: it was not identified. Evidence was also obtained which suggested that the pain of angina was due to a similar mechanism. Further work on skin tenderness led to Lewis postulating the existence of a new system of nerves which were called by him " nocifensor nerves." These researches were published in book form (*Pain*) in 1942. In 1941 Lewis was awarded the Copley Medal of the Royal Society and in 1945 the Conway Evans Prize.

In addition to the study of specially selected patients, Lewis continued to see hospital patients suffering from all kinds of cardiovascular diseases. As a result of this he published two

more books, *Diseases of the Heart* in 1933 and *Vascular Disorders of the Limbs* in 1937. They were designed for clinical use and contained much that was new.

All this time Lewis had been considering how he could foster and perpetuate such work as he was successfully accomplishing. He set himself to attract young men to his way of life and thinking, and published two books, *Clinical Science, Illustrated by Personal Experience* (1934) and *Research in Medicine and other Addresses* (1938) which gave expression to his creed. He ensured that opportunities were available for those wishing to carry out clinical research, by scholarships, grants, and by the establishment in other hospitals of departments like his own. In 1937 the financial support of his appointment was transferred to a Trust endowed by the Rockefeller Foundation. At the same time, he founded the Medical Research Society as a meeting ground for critical discussion and the promotion of friendship among those engaged in clinical research, and was its first chairman. He maintained a close contact with the Cardiac Club which was founded in 1922; and was Chairman at its first meeting in London that year. He had agreed to be chairman at the annual meeting of its successor the Cardiac Society in 1945, but wrote some little time before his death regretting that he would not be well enough to do so. When the Cardiac Society decided to start the *British Heart Journal* in 1939 they were pleased to have a Foreword written by him as a welcome start. In 1933 he had changed the title of his journal *Heart* to that of *Clinical Science* and passed the control of the journal into the hands of the Medical Research Society in 1938, though he remained editor till 1944.

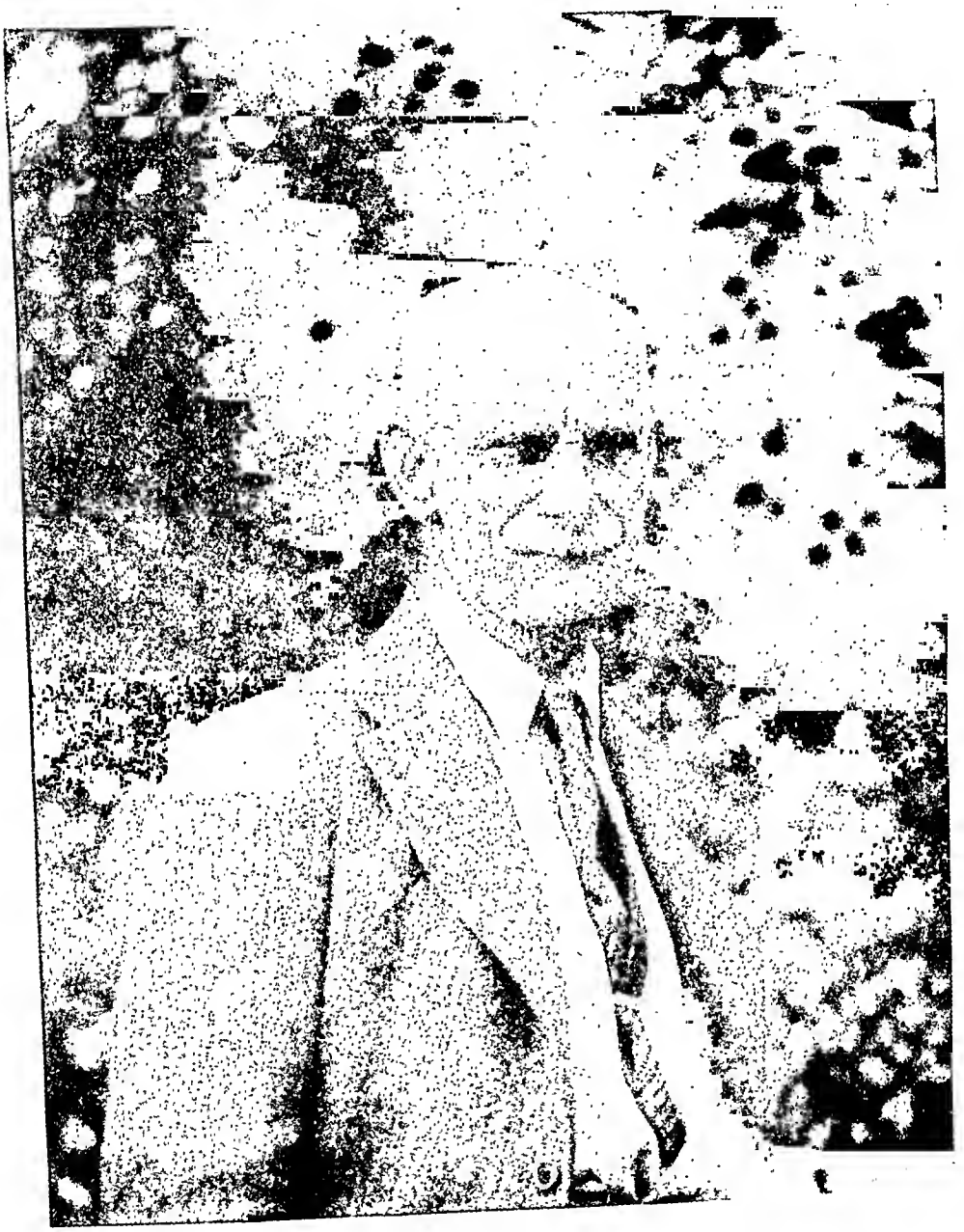
When the Second World War broke out he tried to pursue research in relation to war needs, but could not find an opportunity. He therefore took on more teaching to free others, and carried on with his researches, but towards the end of 1944 his health broke down again (he had had a second attack of coronary thrombosis in 1935), and he died in the spring of 1945. He was buried at Llangorst Church, Llangasty, Brecon.

In such a small compass it is not possible to give more than the barest outline of his achievements. He published about 230 papers in all and wrote 12 books. He disciplined himself to write in a clear and concise style and in later life could write swiftly and without amendment. He took the greatest care in his writings to present all the evidence, not wishing that anything should be accepted on his authority alone. As an editor he insisted on a very high standard from all his contributors. Many received their manuscripts back for revision with some dismay at the number of pencilled alterations. Those who went through them personally with him had a trying ordeal. Some complained that the individuality of the author became lost but most recognized the great improvement that came from his criticisms.

As a teacher he had the faculty of making difficult subjects clear and interesting. He always developed his story in a simple and logical manner and tried to instil into his students the power of observation and reasoning. He was interested in medical education and as late as last year he published an article in the *Lancet* outlining his views.

To cardiologists he will chiefly be remembered during the years up to 1935. He was not an impressive figure in those early days. He was of medium height, spare built, active and tireless. Two characteristics arrested attention, the penetrating look of his deep blue eyes and his quiet voice. He was then in full health, working with unremitting energy year after year, for ten months on end. Problem after problem was attacked in the laboratory, information continually collected in the clinic, which gave knowledge not only to the advanced student but to those dealing with the diagnosis, prognosis, and treatment of cardiac disease. He grudged every minute not spent on his actual problems. Public holidays, committees, discussions on general scientific problems, small talk, were all disregarded if he felt they interfered with the speed of his work. He was capable of driving himself at high pressure and expected the same of his co-workers. They found the pace terrific, and knew there could be no respite till the specific problem in hand was solved or he went away for his annual holiday. Then, for two months on end, he gave the same energy and enthusiasm to watching and photographing birds. In this, as in many other aspects of his life, he received much help and encouragement from his wife (whom he married in 1916); and many will remember the beautiful photographs they saw when they visited him in his delightful home.

To work with him revealed his great characteristics, which were not always evident to those who knew him slightly. A man of contrasts, he was difficult to know well and difficult



THOMAS LEWIS

to understand. He was a humble-minded man, entirely honest, and ready to give help to all those who sincerely asked for it, and able to talk freely on many scientific subjects. He was at the same time a man of great reserve and singleness of purpose. In consequence, when he was immersed in a problem, his impatience, hardness, hatred of slipshod work, and his outspoken manner were not understood by those who did not appreciate his way of life; a sense of ruthlessness was in his work. He resented ill-formed criticism, and defended his views vigorously, but when he was convinced that proper evidence had been brought forward from the newer view, he accepted it without question, for he venerated the truth. He not only won universal admiration for his scientific achievements, but all his associates had a great personal regard for him.

In 1929 thirty-seven of his colleagues (all who had worked with him at University College up to that date) gave him a volume of their photographs and in a letter expressed their thanks for his help by teaching and example and for his many acts of kindness. This gift, arising as a spontaneous expression of their high regard for him, gave him great pleasure. Had this gift been delayed till much later, and had it been possible to include all those who had benefited by his example and teaching, it would have been an immense volume. It has fallen to few scientists to achieve so much and to have had such a profound influence upon the subjects which they have fostered.

A. N. DRURY
R. T. GRANT

Lewis can scarcely be regarded as a pupil of Mackenzie; rather he was already trained, scientifically mature, and well fitted to extend and consolidate the modern conception of cardiac disease which began in Britain early this century. Let us say that Mackenzie was passionately dissatisfied with what he could tell and what he could do for his patients, and so he bent his powerful mind to research mostly by observation. He recognized the calibre of Lewis and persuaded him that here was the opportunity for his talent. Observation was not enough, planned scientific experiment was essential, the electrocardiograph was available, and Lewis started on his course. In no hurry, patiently and steadfastly, he forgot himself in this great work on cardiac physiology, animal and human. I like to think it was Mackenzie, a practitioner of medicine, who coloured the physiology of Lewis to a human tint. However that may be, Lewis was not to be confined to the laboratory, but went to the out-patient department and the wards. He felt it natural that the scientific method should be applied to research in practical medicine, that medicine itself should be directed and developed by clinical science.

Thinkers are not common, and when a thinker is also a doer you have a rare combination. Meeting Lewis was not always easy, though later it became easier. His modesty could not hide the fact that he was indeed superior—a superman of a wholesome kind. He had a reserved manner in social contact, suggesting that his energy was concentrated so much on his life's work that little interest remained for casual visitors or acquaintances. With closer contact, however, anyone showing real interest and a willingness to be corrected, would not fail to receive help and encouragement. His standards were set high, personally and editorially. Did he not once reject for *Heart* a paper from Mackenzie, who took it in good part after the first shock?

As a writer of precise and lucid English, carefully adapted to scientific work, Lewis was also distinguished. He had something to explain or to tell, and he left no doubt as to his meaning. More remarkable is the fact that one man could so combine physiological knowledge with a grasp of the essentials of medical teaching and practice. His brief *Diseases of the Heart* is sufficient proof of this blend of scientist and clinician.

Our feeling about Sir Thomas Lewis might be expressed as gratitude and pride that we have had with us so great and so good a man who dedicated himself to the service of humanity, and chose the field of cardiology and of clinical science.

JOHN PARKINSON

THE MECHANISM OF THE WENCKEBACH TYPE OF A-V BLOCK

BY

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Received August 24, 1945

The Wenckebach type of auriculo-ventricular block is characterized by a progressive lengthening of the A-V conduction time, ending in a completely blocked auricular complex—the Wenckebach period. These periodically recurring dropped beats were first recognized clinically by Wenckebach in 1899 from a careful analysis of radial arteriograms; Engelmann (1896) had noted the same phenomenon in the frog's heart a few years earlier. Changing conduction times, due to varying degrees of recovery of the A-V junction, were postulated by them to account for the dropped beats. A typical feature of the progressive prolongation of the P–R interval is that the most marked increase in the conduction time is seen in the second complex of the group. Later ones show only slightly greater prolongation. The shortest A-V conduction time is seen in the first complex after the dropped beat; i.e. following the longest pause or the longest R–P interval.

Clinically, the Wenckebach type of A-V block is seen especially in digitalis poisoning, in infective myocarditis, due particularly to rheumatic fever and diphtheria, in myocardial fibrosis or infarction due to coronary artery disease, and occasionally in other lesions of the conduction system. It occurs at low auricular rates, most often under the influence of digitalis, or at the high auricular rates of paroxysmal tachycardia (Wenckebach and Winterberg, 1927; Decherd, *et al.*, 1943). A-V block, often of the Wenckebach type, has been produced experimentally by increasing the auricular rate (von Kries, 1902; Erlanger, 1906; Lewis, White, and Meakins, 1913; Lewis and Master, 1925; Ashman, 1925), by vagus stimulation (Mines, 1914; Lewis, 1925; Rothberger, 1931), by cold (Ganter and Zahn, 1912), by pressure (Gaskell, 1882; Erlanger and Blackman, 1909), by ischæmia (Engelmann, 1896), by asphyxia (Lewis and Mathison, 1910; Lewis, White, and Meakins, 1913), by acidosis (Mines, 1913), by various glucosides (W. Straub, 1901; Alcock and Meyer, 1903), by vagomimetic drugs (Starr, 1936; Decherd and Ruskin, 1943), by auricular ectopic beats (Erlanger, 1906; Rothberger 1931; Zeisler, 1931; Schellong, 1931) and by interpolated ventricular ectopic beats (de Boer, 1915; H. Straub, 1918).

The intimate cellular processes that underlie conduction of myocardial excitation are at present obscure; the same obscurity of the fundamental mechanisms involved applies to defective conduction or heart block. The simple physiological properties of excitability, conductivity, refractoriness, and the like are, however, susceptible to study, and it is in such terms that the problems associated with complete or incomplete conduction must be discussed.

Various explanations of Wenckebach periods, which Wenckebach (1899) himself compared to the Luciani periods of rhythmicity of the markedly depressed heart, have been proposed from time to time. W. Straub (1901) produced Wenckebach periods and 2 : 1 A-V block in the isolated frog heart by means of antiarin, and likewise explained these phenomena in terms of decreased excitability or increased refractoriness of the ventricle to regular stimuli. Von Kries (1902) produced Wenckebach periods and 2 : 1 A-V block by warming the auricle and cooling the ventricle, and explained them in terms of the arrival of auricular stimuli earlier and earlier in ventricular diastole and the ventricular refractory

period, thus interfering with ventricular recovery. Trendelenburg (1903) produced Wenckebach periods in ventricular muscle strips, presumably lacking specialized conduction fibres, by increasing the frequency of electrical stimulation, and felt that variable latency was responsible for the block, not diminished conductivity. Hering (1904) invoked the diastolic recovery of reactivity, or Reaktionsbereitschaft, of the ventricular muscle, linking in this term the myocardial properties of irritability, conductivity, and contractility. A rise in auricular rate, diminution of ventricular excitability, or a fall in stimulus strength could, in his opinion, delay the recovery of the ventricular muscle and increase its refractory phase to auricular stimuli, with the production of dropped beats.

The idea of ventricular latency elaborated by Erlanger (1906, 1912), had to be abandoned when Hering (1910) and later workers (Lewis, White, and Meakins, 1913; Lewis and Master, 1925) localized the delay in A-V conduction within the A-V node, probably at the junction of its auricular and ventricular components (Kung and Mobitz, 1930). Mobitz (1924) centered the latency, which he related to the refractory phase of electrical excitability, in the A-V node. Variable A-V conductivity, in his opinion, resulted from variable A-V nodal latency, since he found the difference between maximum and minimum latency was greater than A-V conduction time, and felt, contrary to Lewis (1912), that all parts of the heart conducted at the same rate. He also based his conclusions upon a cryptic interpretation of two types of recovery curves. Gilson (1942) has lately proposed an " excitation time " theory of A-V delay to take the place of the latency theory.

Mobitz' more important contribution was the first recovery curve of conductivity, drawn from an electrocardiogram with a varying auricular rate, showing the reciprocal relation of P–R to the preceding R–P intervals. From the logarithmic curve, which our curves closely resemble, he pointed out that recovery is fastest in the earliest portion of the relative refractory period, and slowest at the end.

Schellong (1924) published a series of experiments on normal and digitalized ventricular strips of the frog heart, which were partially divided or pressed into a bridge simulating the A-V junction. He drew recovery curves of excitability, which closely resembled those of stimulus propagation (Erregungsfortpflanzung), thus linking the properties of conductivity and excitability. Whereas rhythmical stimulation of normal muscle strips caused no decrease in excitability, so that all stimuli were conducted, similar stimulation of digitalized strips resulted in partial block with Wenckebach periods. He concluded that digitalis delayed the recovery of excitability, so that successive stimuli fell earlier and earlier in the relative refractory period, resulting finally in a dropped beat. He postulated, therefore, that frequency of stimulation and the presence of a relative refractory period were the two factors underlying the Wenckebach type of block. He also pointed out that the period of electrical latency was less than 0·002–0·004 sec.; furthermore, that the latency between the auricle and the A-V node was measurable only when the stimulus was minimal, whereas the physiological stimuli were actually four to five times the threshold strength.

Samoiloff (1929) has attempted to explain the production of the Wenckebach type of block in ventricular bridges in terms of gradual prolongation of the absolute and relative refractory periods. Lewis and Master (1925) have demonstrated the lengthening of the refractory periods of the A-V tissues with slower auricular rates, and on this basis, and the shorter preceding recovery period, explained the maximum prolongation of the P–R interval in the second conducted beat of the Wenckebach period. Ashman (1925) plotted curves of recovery of conductivity in turtle heart muscle compressed at the A-V junction. The longer the interval between break shocks to the auricle, the shorter was the A-V interval. The latter increased as the rest period between stimuli became shorter than that permitting complete recovery, and finally 2 : 1 A-V block resulted. Whether this point was the absolute refractory period of conductivity or represented a certain inimical concentration of hydrogen ions, as Mines (1913) supposed, was left an open question by Ashman, and still remains so.

Mobitz (1924, 1928) defined the Wenckebach type of A-V block as Type I, usually functional in pathogenesis, and adduced evidence to show that Type II, known now as the Mobitz type, in which dropped beats occur without previous prolongation of the P–R interval, is usually due to organic interruption of the A-V junction. However, he admitted the not infrequent association of the two types in the same record. Experimentally it has also been

pointed out that transitions from Type I to II may be obtained by increasing the rate of stimulation in digitalized ventricular strips (Schellong, 1924) and likewise in the A-V node and bundle (Scherf and Shookhoff, 1925). Even Wenckebach (1903, 1906), however, leaned toward a different explanation for Type II block, viz., diminished excitability. This explanation has been championed by Hay (1906) for both types of A-V block, and recently accepted as one factor by Campbell (1943).

Heim (1936) published recovery curves based upon Shellong's work (1924) with digitalized frog ventricle muscle strips, and compared them with curves, drawn separately for each Wenckebach period, from patients with Wenckeback type of A-V block due to digitalis administration. In both he frequently found a relatively vertical part of the recovery curve in the middle of the Wenckebach period, in which the P–R interval was prolonged without any marked shortening of the R–P interval. He interpreted this to mean sudden prolongation of the absolute and relative refractory periods from beat to beat. Blumberger (1937) has also drawn similar recovery curves of conductivity in two cases of Wenckebach block, which purported to show some changes in refractoriness from beat to beat.

We have published (1943) recovery curves in a case of reciprocal rhythm, showing the effects of various chemical and nervous influences on the A-V node. In general they resembled the recovery curves of Mobitz (1924), Lewis and Master (1925), Ashman (1925), and Schellong (1924, 1931) in their logarithmic form and absence of momentary variations of any great degree. We have seen such momentary variations in refractoriness in one case (1944), but do not believe that they are the basic mechanism that leads to Wenckebach periods.

Results. (A) Recovery Curves from Clinical Cases

Diagrams that represent recovery of A-V conductivity may readily be constructed by plotting the P–R interval against the preceding R–P interval. These values are obviously not exact measurements of either the conduction time through the A-V node, or the recovery time of these tissues, since they include the time intervals required for the passage of each impulse from the S-A node to the A-V node, and also that required for transmission from the A-V node to the ventricular muscle. Hence the curves obtained are at best approximations, but since the errors involved are probably reasonably constant, the approximations may be regarded as satisfactory and usable.

In general, recovery curves obtained in this fashion are logarithmic in contour. There are many factors that vary from case to case. Our files contain about 50 cases showing partial heart block of the Wenckebach type. In most instances, the patients had had rheumatic or arteriosclerotic heart disease, occasionally with recent myocardial infarction, or had been given digitalis, often in excessive amounts. Digitalis over-dosage was also a factor in the precipitation of paroxysmal auricular tachycardia in a large series of cases previously reported (1943), many of whom showed the Wenckebach type of block, a fact that suggested to us the importance of the auricular rate in the pathogenesis of heart block. In 30 cases, and often in multiple curves, the P waves were sufficiently clear-cut to allow the measurements necessary for the construction of recovery curves. In Fig. 1 we have assembled several of these curves for the purpose of illustrating two points: (1) the individual curves are smooth, without the humps described by Heim (1936) and Blumberger (1937); and (2) the curves show, as a group, tremendous variation in contour and position in the co-ordinate system. Fig. 2 shows curves drawn for consecutive Wenckebach periods in three patients. They illustrate further our failure to observe the type of curve shown by Blumberger and Heim. They also serve to show that whereas the general type of the curve is smooth and constant from moment to moment, the individual points show sufficient variation to indicate that minor influences may affect the exact extent of recovery during each cardiac cycle. These play roles difficult to evaluate, but we consider them in general unimportant in comparison with the physiological attributes of the conduction tissue that are expressed by the recovery curve.

Ventricular premature beats, as is well known, may affect subsequent A-V conduction. Thus in the middle curve of Fig. 2, a point obtained from a cycle following a ventricular premature beat shows much delayed conduction. Conversely, improved conductivity is seen in the location of points above and to the left of the curve when Wenckebach block

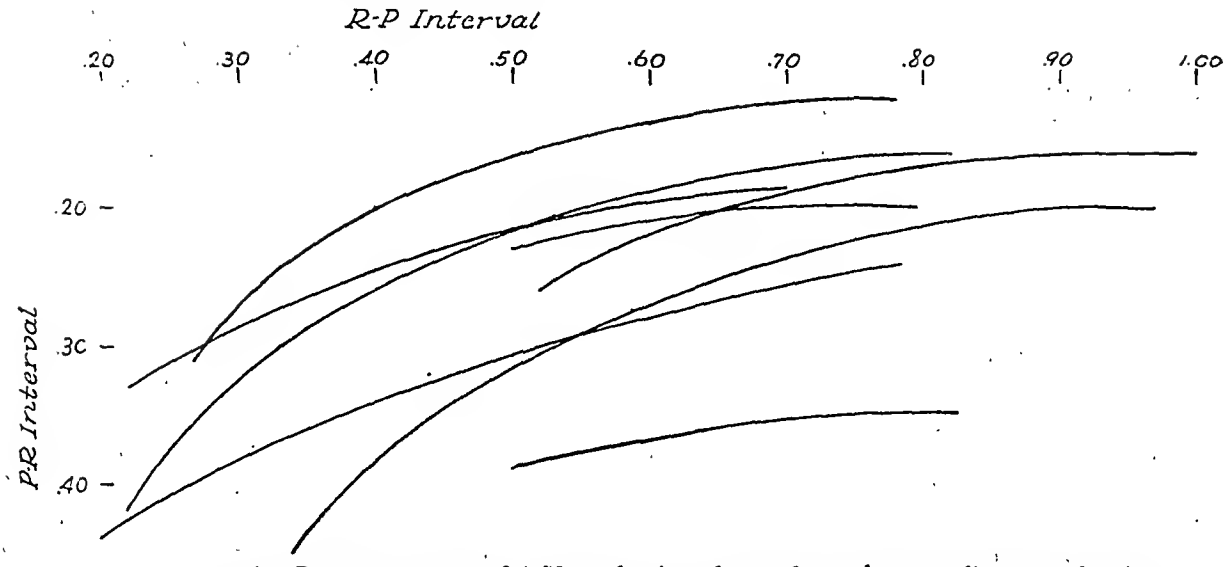

FIG. 1.—Recovery curves of A-V conduction, drawn from electrocardiograms showing the Wenckebach type of block, by relating the P–R intervals to the preceding R–P interval.

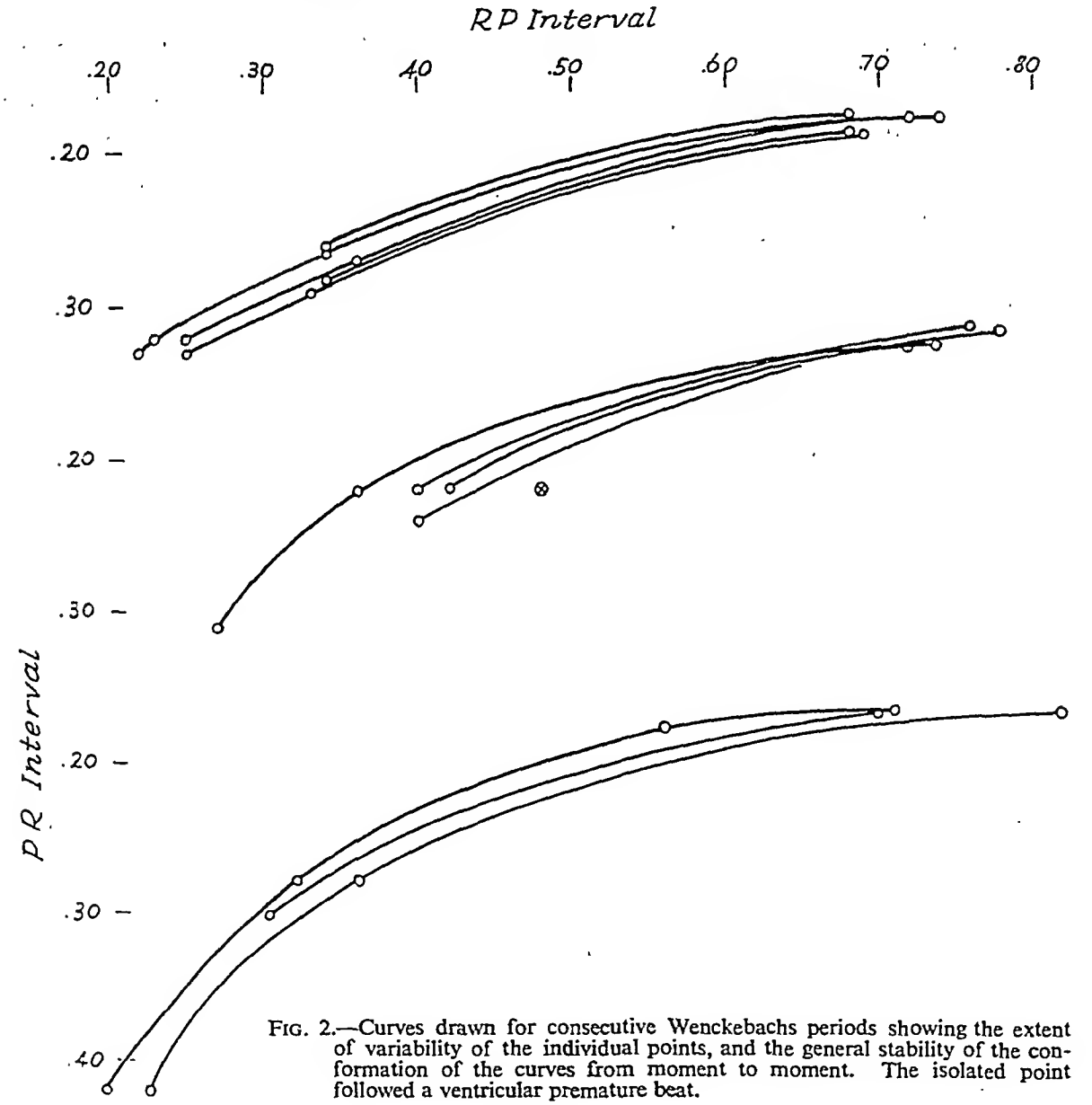

FIG. 2.—Curves drawn for consecutive Wenckebachs periods showing the extent of variability of the individual points, and the general stability of the conformation of the curves from moment to moment. The isolated point followed a ventricular premature beat.

suddenly changes to 1 : 1 conduction, possibly through reflex diminution in vagal tone. It seems probable that the exact location of each point may be slightly affected by reflex vagal and sympathetic influences, the respiratory cycle, the carotid sinus reflex, and cyclic local metabolic changes. Although these and similar factors may—and undoubtedly do—produce minor changes in refractoriness, recovery, and conductivity, we do not believe that they are fundamental to the mechanism that leads to the Wenckebach type of block.

(B) Theoretical Recovery Curves

Inspection of recovery curves derived from clinical cases exhibiting the Wenckebach phenomenon reveals a wide variation in several particulars: the absolute refractory period, the contour of the curve during recovery, the time required for complete recovery, and the conduction time after complete recovery. It is obvious that an additional variable factor, i.e. the auricular rate, must also govern the time available for recovery of the conducting tissues, and hence affect the degree of A-V block. These considerations have led us to select four arbitrarily drawn recovery curves, all with the same absolute refractory period of 0·20 sec., and the same conduction time of 0·20 sec. after complete recovery, but with slopes varying from rapid to slow recovery. Using each curve, the effect of varying auricular rate upon the P–R interval has been studied.

As a starting point for each set of calculations, the assumption has been made that a blocked impulse has fallen just within the absolute refractory period, 0·19 sec. after the preceding R wave. This allows the further assumption of a maximal rest period before the set of complexes with which calculations are begun. In other words, an initial R–P interval is assumed of 0·19 sec. plus the P–P interval being studied. With these premises, the theoretical recovery curves in Fig. 3 have been used to calculate the A-V conduction times for many different auricular rates by reading from the curve the P–R interval that corresponds to each R–P interval. Several examples will make this procedure clear.

1. Curve A; auricular rate 80 a minute (P–P interval 0·75 sec.); maximal possible recovery time 0·75+0·19, or 0·94 sec.

R–P interval	P–R interval	Next R–P interval
0·94	0·20	0·75−0·20=0·55
0·55	0·20	0·55
0·55	0·20	etc., . . .

Hence, at this auricular rate, the P–R interval will always be 0·20 sec.

2. Curve A; auricular rate 109 a minute (P–P interval 0·55 sec.); maximal possible recovery time 0·55+0·19, or 0·74 sec.

R–P interval	P–R interval	Next R–P interval
0·74	0·20	0·55−0·20 =0·35
0·35	0·217	0·55−0·217=0·333
0·333	0·224	0·55−0·224=0·326
0·326	0·227	0·55−0·227=0·323
0·323	0·228	0·55−0·228=0·322
0·322	0·228	0·55−0·228=0·322
0·322	0·228	etc. . . .

Hence, at this auricular rate, the P–R interval will become stabilized at 0·228 sec.

3. Curve A; auricular rate 120 a minute (P–P interval 0·50 sec.); maximal possible recovery time 0·50+0·19, or 0·69 sec.

R–P interval	P–R interval	Next R–P interval
0·69	0·20	0·50−0·20 =0·30
0·30	0·24	0·50−0·24 =0·26
0·26	0·267	0·50−0·267=0·233
0·233	0·295	0·50−0·295=0·205
0·205	0·36	0·50−0·36 =0·14
0·14	blocked	0·50+0·14 =0·64
0·64	0·20	0·50−0·20 =0·30
0·30	0·24	etc. . . .

Hence, at this auricular rate, there is a 6 : 5 A–V block of the Wenckebach type.

4. Curve D; auricular rate 102 a minute (P–P interval 0·59 sec.); maximal possible recovery time 0·59+0·19, or 0·78 sec.).

R–P interval	P–R interval	Next R–P interval
0·78	0·20	0·59−0·20 =0·39
0·39	0·312	0·59−0·312=0·278
0·278	0·362	0·59−0·362=0·228
0·228	0·385	0·59−0·385=0·205
0·205	0·397	0·59−0·397=0·193
0·193	blocked	0·59+0·193=0·783
0·783	0·20	etc. . . .

Using curve D, 6 : 5 block occurs at a slower auricular rate than for Curve A.

5. Curve D, auricular rate 120 a minute (P–P interval 0·50 sec.); maximal possible recovery time 0·50+0·19, or 0·69 sec.

R–P interval	P–R interval	Next R–P interval
0·69	0·20	0·50−0·20 =0·30
0·30	0·352	0·50−0·352=0·148
0·148	blocked	0·50+0·148=0·648
0·648	0·217	0·50−0·217=0·283
0·283	0·36	0·50−0·36 =0·14
0·14	blocked	0·50+0·14 =0·64
0·64	0·219	etc. . . .

Using Curve D, this auricular rate results in a 3 : 2 Wenckebach block.

Table I summarizes the data obtained in this fashion for each curve, and over a wide range of auricular rates.

Comparison of the theoretical curves in Fig. 3 with the curves from clinical sources in Fig. 1, indicates that much longer refractory periods and less complete recovery than has been assumed in constructing Fig. 3 are commonly encountered clinically. For example, if we assume, as seems well justified by Fig. 1, an absolute refractory period of 0·40 sec., and a P–R interval of 0·30 sec. at complete recovery, and employ a curve of the contour of curve D, we find that similar grades of block are obtained with much lower auricular rates.

6. Curve D, auricular rate 67·5 a minute (P–P interval 0·89 sec.); maximal possible recovery time 0·89+0·39, or 1·28 sec.

R–P interval	P–R interval	Next R–P interval
1·28	0·30	0·89−0·30 =0·59
0·59	0·412	0·89−0·412=0·478
0·478	0·462	0·89−0·462=0·428
0·428	0·485	0·89−0·485=0·405
0·405	0·497	0·89−0·497=0·393
0·393	blocked	0·89+0·393=1·283
1·283	0·30	etc. . . .

These physiological constants produce a 6 : 5 block at a slower auricular rate than in example 4.

7. Curve D, auricular rate 75 a minute (P–P interval 0·80 sec.); maximal possible recovery time 0·80+0·39, or 1·19 sec..

R–P interval	P–R interval	Next R–P interval
1·19	0·30	0·80−0·30 =0·50
0·50	0·452	0·80−0·452=0·348
0·348	blocked	0·80+0·348=1·148
1·148	0·30	etc. . . .

Hence, we derive a 3 : 2 block at this auricular rate, which is much slower than in example 5.

These examples suffice to show that the grades of block listed in Table I may readily be anticipated at auricular rates well within the range of those observed clinically.

Similar depression of the conducting tissues with prolonged refractoriness and delayed recovery will account for the presence of the higher grades of A-V block at auricular rates much lower than those required in Table I. An absolute refractory period of 0·60 sec., and a P–R interval at complete recovery of 0·40 sec., permits the calculation of a block as high as 6 : 1. We have encountered (1943) one example of 6 : 1 block in a patient with paroxysmal tachycardia whose conducting tissues were reflexly depressed by carotid sinus pressure.

To return to Table I, certain general observations should be made.

TABLE I

CALCULATED DEGREE OF A-V BLOCK FOR VARYING AURICULAR RATES

P–P interval	Curve A	Curve B	Curve C	Curve D
0·90				0·20
0·89				0·206
0·85				0·223
0·80			0·20	0·250
0·79			0·202	0·255
0·75			0·213	0·277
0·70		0·20	0·242	0·312
0·69		0·202	0·247	0·327
0·65		0·213	0·287	0·352
0·60	0·20	0·258	0·382	0·398
0·59	0·205	0·277	9 : 8	6 : 5
0·58	0·210	0·322	7 : 6	5 : 4
0·57	0·215	12 : 11	6 : 5	4 : 3
0·56	0·222	8 : 7	5 : 4	4 : 3
0·55	0·228	7 : 6	4 : 3	4 : 3
0·54	0·238	5 : 4	4 : 3	4 : 3
0·53	0·255	5 : 4	4 : 3	3 : 2
0·52	13 : 12	4 : 3	3 : 2	3 : 2
0·51	7 : 6	4 : 3	3 : 2	3 : 2
0·50	6 : 5	4 : 3	3 : 2	3 : 2
0·49	5 : 4	3 : 2	3 : 2	3 : 2
0·48	4 : 3	3 : 2	3 : 2	3 : 2
0·47	4 : 3	3 : 2	3 : 2	3 : 2
0·46	3 : 2	3 : 2	3 : 2	3 : 2×4 2 : 1×1
0·45	3 : 2	3 : 2	3 : 2	3 : 2×1 2 : 1×1 3 : 2×1
0·44	3 : 2	3 : 2	3 : 2	2 : 1×1
0·43	3 : 2	3 : 2	3 : 2×1 2 : 1×1	3 : 2×1 2 : 1×2
0·42	3 : 2	3 : 2	3 : 2×1 2 : 1×1	2 : 1
0·41	3 : 2	3 : 2×1 2 : 1×1	3 : 2×1 2 : 1×1	2 : 1
0·40	3 : 2	3 : 2×1 2 : 1×1	3 : 2×1 2 : 1×3	2 : 1
0·39	2 : 1	2 : 1	2 : 1	2 : 1
0·38	2 : 1	2 : 1	2 : 1	2 : 1
0·37	2 : 1	2 : 1	2 : 1	2 : 1
0·36	2 : 1	2 : 1	2 : 1	2 : 1
0·35	2 : 1	2 : 1	2 : 1	2 : 1
0·34	2 : 1	2 : 1	2 : 1	2 : 1
0·33	2 : 1	2 : 1	2 : 1	2 : 1
0·32	2 : 1	2 : 1	2 : 1	2 : 1
0·31	2 : 1	2 : 1	2 : 1	2 : 1
0·30	2 : 1	2 : 1	2 : 1	2 : 1
0·29	2 : 1	2 : 1	2 : 1×4 3 : 1×1	2 : 1×2 3 : 1×1
0·28	2 : 1	2 : 1×5 3 : 1×1	2 : 1×3 3 : 1×1	2 : 1×1 3 : 1×1
0·27	2 : 1	2 : 1×3 3 : 1×1	2 : 1×2 3 : 1×1	2 : 1×1 3 : 1×1
0·26	2 : 1	2 : 1×2 3 : 1×1	2 : 1×2 3 : 1×1	2 : 1×1 3 : 1×1
0·25	2 : 1	2 : 1×1 3 : 1×1	2 : 1×1 3 : 1×1	2 : 1×1 3 : 1×3
0·24	2 : 1×2 3 : 1×1	2 : 1×1 3 : 1×1	2 : 1×1 3 : 1×2	3 : 1
0·23	2 : 1×1 3 : 1×1	2 : 1×1 3 : 1×2	2 : 1×1 3 : 1×3	3 : 1
0·22	2 : 1×1 3 : 1×1	2 : 1×1 3 : 1×3	3 : 1	3 : 1
0·21	2 : 1×1 3 : 1×3	3 : 1	3 : 1	3 : 1
0·20	3 : 1	3 : 1	3 : 1	3 : 1

TABLE I.—Calculated P–R intervals and grades of A-V block, obtained at the auricular rates indicated, calculated from the curves of Fig. 3 in the manner described in the text. Admixtures of block are indicated; for example, 3 : 2 alternating with 2 : 1 block is listed as 3 : 2×1/2 : 1×1.

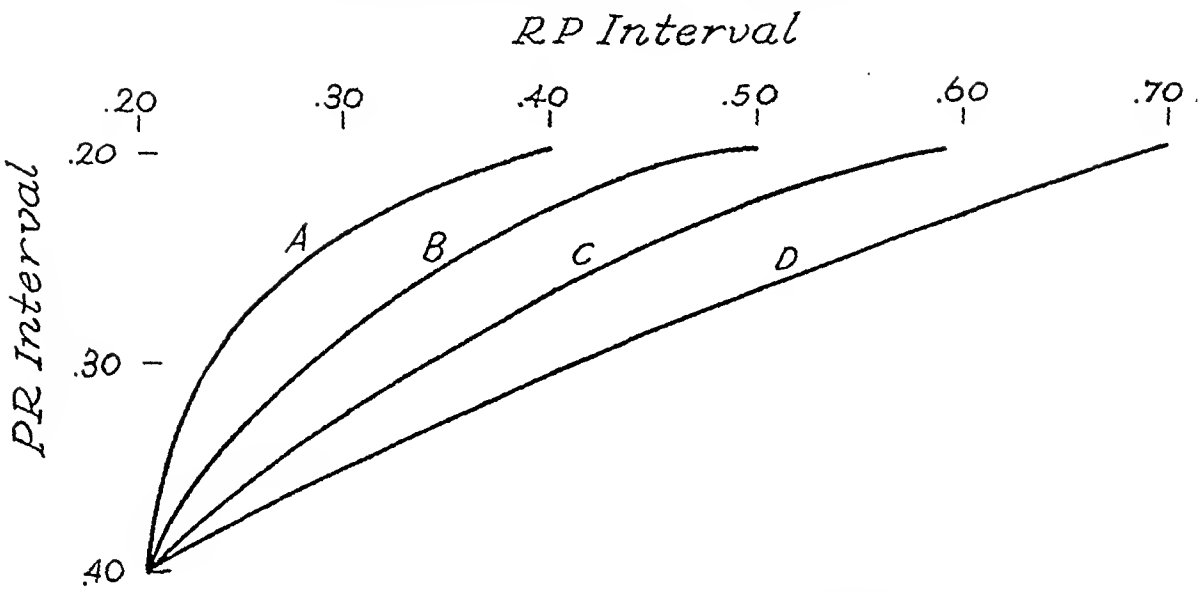

FIG. 3.—Idealized curves, used for the calculations described in the text.

1. Variations in the auricular rate, for each of the recovery curves studied, lead to a wide variety of conduction disturbances. With increasing auricular rates, A-V conduction is progressively impaired.

2. At slow rates, whenever thc P–P interval is such that the resulting R–P interval falls in the range of complete recovery, the P–R interval is normal.

3. At slightly faster rates, whenever the resultant R–P interval falls in the range of partial refractoriness, or incomplete recovery, there is partial heart block with prolongation of the P–R interval. This is longer with the curves of less rapid recovery, i.e. longest with curve D. The limiting factor is the P–R interval at R–P intervals just exceeding the refractory period, and with our curves could not exceed 0·40 sec. Under other conditions, the longest P–R interval without dropped beats could be longer than 0·40 sec., and, of course, not infrequently is much greater. As the curves show progressively slower recovery, prolongation of the P–R interval without dropped beats is possible only at slower and slower rates, since dropped beats occur more readily.

4. Further shortening of the P–P interval leads to low grade A-V block, with dropped beats of the Wenckebach type. At any given auricular rate in this range, the degree of block is higher as we pass from curve A to curve D.

5. As the P–P interval is further shortened, 2 : 1 block is found, first mixed in varying proportions with 3 : 2 block, and then for a wide span of auricular rates as simple 2 : 1 block. At still higher auricular rates 3 : 1 block appears, first in admixture with 2 : 1 block, and finally, alone.

6. At any auricular rate, the grade of block is highest with curve D, which shows slowest recovery. Even higher grades of block, at the same auricular rate, may be found if the curve D is shifted down and to the right in the direction of further depression of conductivity and recovery. This is shown in examples 6 and 7, above.

7. In general, the flatter the contour of the recovery curve, as in curves C and D, the more typical of the classical Wenckebach period are the consecutive P–R intervals. This is illustrated in example 4 above, derived from curve D, which is to be contrasted with example 3, derived from curve A. In the latter, the greatest prolongation of the P–R interval is seen at the end of the Wenckebach cycle, just before the dropped beat; in the former, the P–R intervals show typically the greatest increase in the second complex of the group. This is consistently borne out in all of the calculations upon which Table I is based. This is due to the fact that near the absolute refractory period, curve A has a more vertical slope than curve D.

Comment

Cardiac physiologists have variously attempted to explain the Wenckebach type of partial heart block on the basis of changing properties of the conducting tissues. They have postulated momentary changes in excitability, latency, the absolute or relative refractory periods, recovery of excitability or of conductivity, and increasing rate of stimulation, produced by experimental factors, drugs, or myocardial disease. The latency theory is no longer considered tenable; possible changes in excitability are not accessible to clinical study; nor do we believe that momentary changes in refractoriness or conductivity need be invoked to explain the mechanism of Wenckebach block. The role of certain of the physiological properties of the heart muscle has been appreciated, but a unified concept has hitherto been lacking. Schellong was clearly aware of the importance of the relative refractory period as reflected in the recovery curve of excitability, and of the frequency of stimulation. Mobitz and Ashman demonstrated the effect upon the P–R interval of the preceding recovery time. Numerous authors have emphasized the importance of increasing auricular rates.

Studies of clinical material permit the evaluation of the following factors that determine the sequence of A-V conduction in the Wenckebach type of block:

1. Duration of complete refractoriness.
2. Duration of partial refractoriness.
3. Contour of the recovery curve.
4. Conduction time after complete recovery.
5. Auricular rate (P–P interval).

It should be emphasized that the first four factors listed actually are encompassed by the curves of recovery of A-V conductivity. For this reason we consider these curves fundamental to any attempt at explanation of Wenckebach block. We have demonstrated above that all varieties of Wenckebach block may be deduced by varying these five factors, i.e. the recovery curve and the auricular rate. In fact, other varieties of partial A-V block seem to be susceptible to explanation on the same basis (Table I).

The curves of Fig. 3 are not purely artificial; they are idealizations of the several varieties of curves that were drawn from clinical cases, and represent some of the possible fluctuations in speed and completeness of recovery. Their contour and co-ordinate values are typical of many of the recovery curves published previously, both by ourselves and other authors. By assuming certain auricular rates, curves may be drawn from Campbell's formula (1943) for the length of consecutive P–R intervals; these resemble our curve C or, to a lesser extent, curve B. The admixture in all proportions of closely adjoining grades of block, such as 3 : 2 with 2 : 1, or 2 : 1 with 3 : 1, seen in Table I, is also encountered clinically. The frequency with which the various grades of block are found in Table I, as well as their stability over a wide range of auricular rates, agree well with clinical experience.

Cases are encountered clinically that show marked transitions in the grade of block, sometimes cyclic in character, e.g. from 4 : 3 to 2 : 1, or from 3 : 2 to 1 : 1, and back again. These shifts cannot be deduced from a single recovery curve, and require the assumption of transient change in those myocardial properties that fix the recovery curve. These changes in refractoriness and recovery and, equally important, in the auricular rate—may be due to a wide variety of chemical or reflex nervous factors. Similar factors, as we have pointed out above, may well be responsible for the minor deviations of individual points from the smooth recovery curves of clinical cases. The point at which these otherwise minor deviations are most conspicuous is at the absolute refractory period, where there may be some overlapping of the R–P intervals of conducted and dropped beats.

The five factors that we have listed above, which determine the character of the Wenckebach periods, are mutually interdependent and may change simultaneously in the same or opposite directions. Thus, acceleration of the auricular rate, which would tend to increase A-V block, in itself shortens refractoriness and recovery (Lewis and Master, 1925), in effect shifting the recovery curve upwards and to the left. Increased vagal tone shifts the recovery curve in the direction of less rapid recovery and greater block, but may be associated with a slower auricular rate, which would allow more complete recovery. These momentary shifts in refractoriness from beat to beat, correlated with changing recovery times, have

served Lewis and Master, and Rothberger as the entire basis for their explanations of Wenckebach block. Our data show it is unnecessary to invoke such shifts to explain the Wenckebach phenomenon.

Aside from these minor variations, the recovery curve of the typical case of Wenckebach block is smooth in contour, and shows remarkable stability in the absolute and relative refractory periods, and in the A-V conduction time after complete recovery. Under these circumstances, variations in the auricular rate assume paramount importance in determining the grade of block in the Wenckebach periods at any time. Contrary to the reports of Heim and Blumberger, in our experience neither the contour of the recovery curves, nor their place in the co-ordinate system, change significantly from cycle to cycle in the typical case.

On the other hand, the diverse recovery curves of different patients, or of the same patients under different circumstances, account for the varying degrees of block that may occur at the same auricular rate. Thus, with one recovery curve, the P–R interval may reach a maximum of 0·30 sec. before a dropped beat, while with another curve, there may be 1 : 1 conduction with a constant P–R interval of 0·45 sec., or higher. This same type of phenomenon may occur, with a constant recovery curve, as a result of variation in the auricular rate.

It has been noted by other observers, both clinically and experimentally, that the Type II block of Mobitz is occasionally seen in association with the Wenckebach Type I block. Since all varieties of partial A-V block, with the exception of Type II, are seen in Table I to have the same fundamental explanation in terms of the auricular rate and the recovery curve of A-V conduction, it seems probable that Type II would have the same physiological basis. We have had no instance available for study, but we suggest the possibility that this type of block occurs when the recovery curve is an almost horizontal straight line, from the absolute refractory period to the end of recovery. We would predict, if this assumption were true, that minute increments of the P–R interval precede the sudden dropped beat. If this is not true, the explanation must depend on sudden changes in refractoriness of the severely damaged conducting tissues. Sudden changes in excitability seem to us to have no clinical or experimental support or parallel.

The empirical formula developed for Campbell by Professor Rushton for the prediction of consecutive P–R intervals in the average Wenckebach period, serves to emphasize that the block progresses according to a simple logarithmic law. As mentioned previously, logarithmic recovery curves may be drawn from this formula by assuming an auricular rate. This formula fixes the P–R interval at complete recovery, the longest P–R interval before dropped beats occur, and the duration of recovery. For each grade of block, the conformation of the recovery curve is likewise fixed, and as the grade of block decreases, with more rapid ventricular rates, the curves show a shift to the left. However, the formula does not fix the position of the curves in the co-ordinate system, and with this the absolute and relative refractory periods. These vary with the auricular rate assumed. We have been impressed with the wide diversity of the form and position of our clinical recovery curves, as well as the crucial significance of variations in the auricular rate. In the face of so many variables, we have not attempted to formulate a comprehensive mathematical expression for them all.

Summary

The Wenckebach type of partial A-V block is explained on the basis of varying auricular rates and varying curves of recovery of A-V conductivity. Other varieties of partial A-V block seem to be explicable in the same fashion.

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HYPOXÆMIA TESTS IN CORONARY DISEASE

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Received August 4, 1945

Many people have suffered from anginal pain and have still lived to old age. Cardiac infarction may set in suddenly after having been for a long time foreboded by a typical angina pectoris: on the other hand, a person may without any warning whatever fall prey to a lethal infarct. The dramatic character of the picture of the coronary heart disease and its capricious appearance raise the following two questions. How can one make an early diagnosis on the basis of the changes that form the substratum of the disease in order to permit a timely recourse to prophylactic measures? Can refined diagnostic measures dispel the anguish many people feel owing to the dread of this disease? Apart from electrocardiograms common clinical examination is not of much use. The history is the chief factor, but people differ in sensitivity to pain, in the faculty of observation, and in exactness of description. No wonder that attempts have for a long time been made to create a practical and objective method of testing the coronary function. Two principles have been applied in the first place, viz. electrocardiograms after respiration of air lacking in oxygen (by a gas mixture with diminished oxygen pressure or general under pressure), and after exertion.

Since the former method, referred to as the "hypoxæmia* test" by us, has now been employed for more than three years, it has seemed desirable to submit a few preliminary figures collected during the years 1942–44, to supplement the experiences so far available of the test as a practical method in clinical work. For reasons of space, I must limit myself to a statement of the figures without further critical remarks except the most necessary ones.

In 1933, Dietrich and Schwiegk found pathological features in the cardiogram after breathing air deficient in oxygen. Kai Larsen (1938) at Warburg's clinic in Copenhagen, performed 192 hypoxæmia tests on 133 subjects, 28 of whom were healthy and 43 suspected of coronary heart disease. The oxygen percentage in the inspiration air was 9 per cent, the test lasting for 6–8 minutes. As regards cases with coronary symptoms, he found 4 positive tests in 10 instances with a normal cardiogram at rest and 5 positive tests in 10 others with but small changes in the cardiogram at rest; in another 4 cases in the latter group, a positive cardiogram with exertion was noted. In the U.S.A., Levy, Barach, and Bruenn (1938) gave an account of their first investigations regarding the effect of hypoxæmia on the circulation. The work was supplemented in 1940 by Levy, Bruenn, and Williams with studies of the effect of drugs during hypoxæmia tests. Those studies were pursued in 1941 by reports from Levy, Bruenn, Williams, and Carr on 326 tests with 10 per cent oxygen for 20 minutes in 262 cases, 115 of whom were healthy and 147 suffered from cardiac disease, 79 of the latter having suspected or certain coronary heart disease. They obtained from 18 to 69 per cent positive tests, relative to the degree of the coronary symptoms and the appearance of the cardiogram at rest.

In Sweden, Nylin (1943) has earlier presented some data from 163 private patients with 22 per cent positive tests. Åkesson and Malmström (1945) have recently published some cases of cardiograms after exertion when breathing air deficient in oxygen. The hypoxæmia test in one form or another has also been adopted for clinical purposes elsewhere in this country.

* The term hypoxæmia has been used throughout instead of anoxæmia, which is most common in the Anglo-Saxon literature, because the former has been considered more adequate in this connection.

Methods and Grouping of Patients

The material which will be discussed in the present paper comprises 350 hypoxæmia tests carried out on a total of 326 patients examined during the years 1942–44 at the Sabbatsbergs Sjukhus: 166 of these patients were men and 160 women; 43 of the total number of patients were under 30 years of age, 40 between 31–40, 88 between 41–50, 88 between 51–60, 54 between 61–70, and 13 above 70 years of age. In 1942, 87 cases were examined, 8 being positive, i.e. 9 per cent, and in 1943, 140 cases, 20 being positive, i.e. 14 per cent, and in 1944, 114 cases with 20 positive tests, i.e. 17 per cent. The indications for the use of the test have probably been gradually stabilized.

The technique employed here conforms to that adopted by Levy *et al.* (1938, 1940) viz. inspiration of a mixture of 10 per cent oxygen and 90 per cent nitrogen for 20 minutes. Nylin has described the details earlier. The patient, who has not eaten for some hours, is placed on an examination couch and inhales the gas compound through a mouthpiece connected with a Lovén mask while a nose clip is adapted. The patient is informed of the nature of the test, of the discomforts that may appear, and requested to breathe calmly and give a signal with the hand to the assistant if the discomforts should become too severe. A cardiogram is taken at rest before the test and after 20 minutes or earlier if the test should have to be abbreviated. Immediately after the test, the patient is given 100 per cent oxygen-gas for as long as necessary.

The gas mixture was delivered during the first years in bombs containing 10 per cent O_2 and 90 per cent N_2. According to analyses which have been performed, the oxygen content has varied within the limits $10 \pm 0{\cdot}3$ per cent. During the second half of the year 1944, the gas-mixture bomb was replaced by a gas-mixing apparatus, constructed at Aga by Andersson, civil engineer, according to Nylin's directions, the principle of which will be seen in the diagram (Fig. 1). Pure nitrogen gas runs through an injector (3) into a gas current-meter (5)

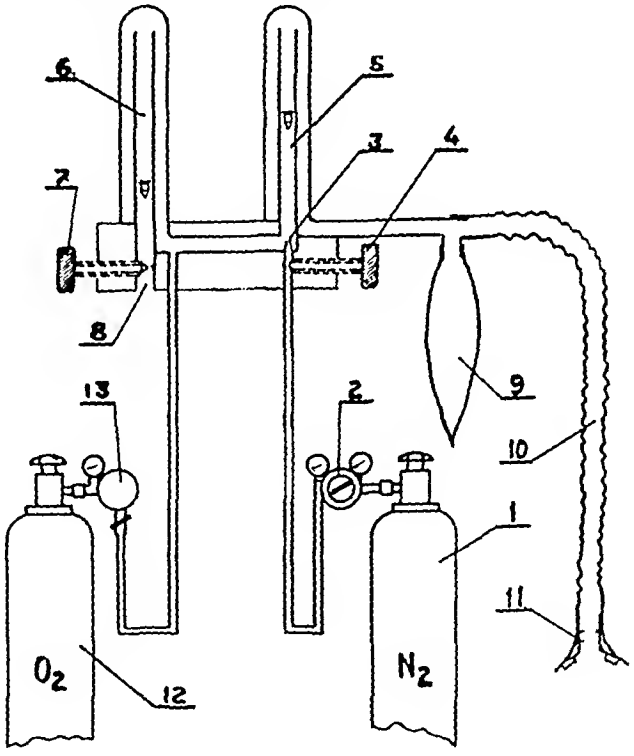

Fig. 1.—Diagram of gas-mixing apparatus (see text).

which draws in by means of suction a quantity of indoor air (8) which can be made equal to the nitrogen gas quantity by manipulation of the floats (4, 7) in the two gas current-meters. Since the hypoxæmia tests are performed in fresh indoor air with an oxygen content of 20 per cent, the oxygen-gas content in the gas mixture will, accordingly, be half of it, i.e.

TABLE I

DETAILS OF HYPOXÆMIA TESTS (1942–44)

	Number of cases				Number of tests												Number of cases									
					Group A Normal rest curve			Group B Coronary rest curve			Group C Cardio-sclerotic rest curve			Group D Other changes in the rest curve			Doubtful tests		Positive tests		Exertion cardiogram			Negative HO but positive EC	Positive HO and positive EC	Positive HO but negative EC
		Number of cases	Men	Women	Negative	Doubtful	Positive	Negative	Doubtful	Positive	Negative	Doubtful	Positive	Negative	Doubtful	Positive	Number	Percentage	Number	Percentage	Negative	Doubtful	Positive			
Healthy somatically		16	11	5	16																10					
Other diseases without coronary disease	79	41	21	20	31	2	1	5	1		1			1			3	7·2	1	2·4	6					
Other diseases with suspected cor. dis.		33	16	17	18	1	3	4	4	2	1			2			5	15·1	5	15·1	6					
Other diseases with probable cor. dis.		5	5		2		1*	1		2*	1								2	40	2		2	1	1	1
Organic heart disease without cor. dis.	31	13	9	4	9				2					2			2	15·4			6					
Organic heart disease with suspected cor. dis.		16	7	9	6	1	1	2		1		1		3		1	1	6·3	4	25	3		2	1	1	
Organic heart disease with probable cor. dis.		2	2		1					1									1	50						
Hypertension without cor. dis.	85	28	12	16	12		1	10	3	1	1			1			3	10·7	2	7·1	2	2	1	1		
Hypertension with suspected cor. dis.		36	12	24	20	1	1	8	1	2	1			1		1	2	5·6	4	11·2	4	1	2	2		
Hypertension with probable cor. dis.		21	9	12	5	2	4*	3	3	4*	1					1*	5	23·8	7	33·3	3					
Other heart disease without cor. dis.	39	26	14	12	14	1	1	2			2			7			1	3·8	1	3·8	9		2	2		
Other heart disease with suspected cor. dis.		13	3	10	6		3*			1*		1		2	1	1	1	7·6	5	38·5	4		3	2	1	
Other heart disease with probable cor. dis.																										
Only symptoms resembling A.P.	66	25	15	10	21			1	1		1			2			1	4·0			4	1	1	1		
Suspected angina pectoris (A.P.)		33	14	19	21	1	5	3	3*	3*							4	12·1	8	24·2	11	1	1		1	
Certain angina pectoris (A.P.)		8	6	2	3	1	1	2	1	1							2	25·0	2	25·0	3		1		1	
Earlier infarction without A.P.	10 (18)	1 (2)	1	(1)				(1)						1												
Earlier infarction with A.P. now		9 (16)	9 (13)	(3)	3		(1)	4 (5)	1 (3)	2 (4)							1 (3)	11·1 18·8	2 (5)	22·2 31·3	4 (6)	(1)	1	1		1
Infarction later in the course	(5)	(5)	(5)		(1)		(1)	(2)	(1)	(1)							(1)	20	(2)	40	(1)					
	326		166	160	188	10	22	45	20	20	9		2	22	1	4	31 cases (31 tests); 74 cases		44 cases (48 tests); (79 tests)		77	5	16 /=98/	11	5	2
I. Healthy and without cor. dis. and the group "only symptoms resembling A.P."	149		82	67	103	3	3	18	7	1	5			14			10	6·7	4	2·7						
II. All cases with suspected coronary symptoms	131		52	79	71	4	13*	17	8*	9**	2		2	7	1	3	13	9·9	26	19·8						
III. All cases with probable or certain coronary symptoms	46		32	14	14	3	6**	10	5	10**	2			1		1*	8	17·4	14	30·4						
	326		166	160	188	10	22	45	20	20	9		2	22	1	4										

Exposing HO tests = Gr. A+C+D.

	Number of cases	Doubtful No.	Doubtful Percentage	Positive No.	Positive Percentage
I.	127	3	2·3	3	2·2
II.	100	5	5·0	18	18·0
III.	26	3	11·5	6	23·1

* = different results of the test in the same pat.
( ) = present already in earlier clin. group.

Number of tests, 350.

cor. dis. = coronary disease.

A.P. = angina pectoris.

10 per cent. The oxygen-gas content obtained by this method will be at least equal in reliability to a ready mixture.

The cardiogram examined has, in practically all cases, also comprised one or several chest leads. In the course of these years, different chest lead procedures have been tried at the clinic. The predominant number of cardiograms have been performed with Nylin's anterior and posterior lead, some also with an inferior lead, as described earlier by Nylin and Grewin (1942). After the stabilization of the chest lead technique to only the anterior and posterior leads, all the five leads have been registered synchronously with the help of Elmqvist's five-lead electrocardiograph.

The indications for the hypoxæmia test have principally occurred in the following cases: suspected coronary cases, a mixed group of undifferentiated cases sent to our clinic for an estimation of the possible risks of operation, and cases from the State Insurance Board. The test has been regarded as contra-indicated in the event of infarcts within six months and in cases with failure. Nor has any patient been subjected to more than one test on one and the same day.

The earlier discussion dealt with, *inter alia*, the risks involved in the test. In this instance, experience has however been favourable. The majority of patients manifest, during the course of the test, a considerable general cyanosis. The deficiency in the oxygen saturation of the blood, as a rule, raises the frequency in the heart of, probably, about 25–40 per cent. Many patients, in fact, feel a moderately severe headache. Thus, these occurrences are to be expected and need not give rise to anxiety in the patient or the conductor of the test. Further, they are rapidly transient when the oxygen-gas has been turned on at the end of the test. As to the possibility of complications, two have occurred in our material, viz. firstly, mild anxiety in very nervous patients, and secondly, attacks of paleness, peripheral chill, bradycardia, sensation of choking, and general appearance of shock. In all likelihood, this is due to a vagal excitation in persons particularly predisposed to it. No technical error has been noted. Recently, two alarming cases of this kind have been observed, but no effect on the cardiogram other than bradycardia was detected. Both cases recovered quickly by means of adequate therapy. In this material a similar picture seems to have occurred in one case, also with a negative result of the test, but, on the other hand, with suspected anginal pains. The cases with a decrease in the heart frequency after 20 minutes may, perhaps, be milder equivalents to the forementioned case. They comprise another 13 with negative tests and one with a positive test. Thirdly, there may, conceivably, involve a risk of eliciting an infarct in a heart where this constitutes a latent threat. We have not been in a position to ascertain any such case, nor have I seen any mention of it in reports on the subject. On the other hand, suspected or typical anginal pains have appeared in 7 cases with positive tests, 6 of which have been interrupted after less than 20 minutes, and in 5 negative cases, 3 of which were interrupted prematurely. Infarction has not ensued from the test in any single case. An infarct was mentioned in the patient's history in one of the positive cases and in one of the negative ones which was interrupted prematurely. According to a newspaper notice, one patient died 13 days after an attempt to perform a hypoxæmia test which had had to be interrupted owing to pain without the registration of any curves. He had suffered from an anterior infarct two years earlier and had been incapable of work for a year on account of pain.

Apart from the first acute stage of a cardiac infarct, the coronary heart disease is more frequently, at the time of the examination, a latent condition than a manifest one. Thus the *raison d'etre* of a hypoxæmia test should be to confirm or remove, objectively and manifestly, any suspicion of the coronary heart disease that there has been reason to entertain on the basis of the patient's history.

Taking this into consideration, the present material has been classified in accordance with the patient's history and such simple clinical data as can be established by any physician, and not according to the clinical diagnosis arrived at after examination of the cardiogram and hypoxæmia tests of the patients concerned. Moreover, when the aim has been to "expose" a latent injury, in a cardiographic respect, a differentiation between the various tests has seemed most adequate in accordance with the appearance of the ordinary curve at rest. As regards the usefulness of the test compared with the ordinary cardiogram, a patho-

logical test after a normal ordinary record is of more importance than an accentuation of the curve of coronary insufficiency. The tests have therefore been divided into 4 groups, as follows: one with a normal cardiogram at rest, one with a coronary curve at rest,* another with a " cardiosclerotic " curve at rest (bundle branch block, low voltage), and, finally, one with some other change in the cardiogram at rest (principally arrhythmias). The test has been denoted as negative, doubtful, or positive, according to the outcome of the test. For practical reasons the following criteria of Levy *et al.* (1941) have been used with, however, a substitution of lead IVF for one of our chest leads.

Criteria for Positive Tests, according to Levy et al. (1941)

The test is positive when

(1) the lowering of the S–T segments in leads I, II, III, and IV F constitutes or exceeds 3 mm., or
(2) T I is inverted, altogether or partly, and the S–T segment in lead I is lowered at least 1 mm., or
(3) T IV is altogether inverted, irrespective of the S–T segment, or
(4) T IV is partly inverted and the S–T segment is lowered at least 1 mm.

Clearly affected tests, not fitting into Levy's scheme, have been referred to a "doubtful" group. Still, the exact tracing of the limits between these groups remains an open question which future follow-up examinations may solve. No definite patho-physiological quantitative correlation to the positive test is as yet known. On the contrary, Vesa's observations as well as our own have shown that considerable spontaneous variations occur on and off with regard to S–T segments and T waves. There is, reasonably, no cause to believe that a certain limit at all exists. The transitions are, probably, vague and therefore a separate group of doubtful tests may, for the time being, be justified, not least in consideration of later follow-up examinations.

The cardiograms have chiefly been studied only with regard to the S–T segments and the T waves. The distance from the extreme points of these parts of the curve to a horizontal line through the lowest level of the P–Q line has been measured within 0·5 mm.† Hypoxæmia tests cannot be estimated without millimetre measurement.

In order to be able to perform off-hand an arrangement of each case in the most correct clinical group with the guidance of the history of the patient and simple clinical data (with the exception of the cardiogram), extracts from the records in this respect have been made on one side of a so-called needle-card, while the cardiographic facts have been annotated on the back. Then, the whole material has been classified simultaneously in order to obtain the greatest possible uniformity. The clinical group has been marked on each card before turning it to analyse the cardiographic changes.

The clinical grouping has been intended to comprise the following cases:

(1) Somatically healthy persons.
(2) Cases of another disease (often consultation cases).
(3) Cases of organic heart disease (valvular diseases and endocarditis or myocarditis.)
(4) Cases of hypertension.
(5) Cases of other heart diseases (principally arrhythmias, thyrotoxicosis, etc.).
(6) Cases with symptoms of angina pectoris, without any other disease.
(7) Cases with earlier cardiac infarct.
(8) Cases with later cardiac infarct (5 cases included in other groups).

The groups 2–5 have been divided into sub-groups with regard to the presence or absence, respectively, of " coronary " symptoms (mainly anginal pains), the latter being denoted as " suspected " or " probable " according to the degree of severity of the symptoms. Group 6 has, almost analogously, been divided into a group with symptoms resembling angina

* This group has also comprised curves with a digitalis effect *or* coronary insufficiency or both.

† It would, of course, be ideal to refer to a horizontal line through the T–P line which constitutes the real iso-electrical line. However, for technical reasons, Larsen as well as Levy, and others, have had to use the P–Q distance as a starting-point for the measurements. This has also been necessary in the present material of curves.

pectoris, but with a very faint suspicion of it, one with more suspicious symptoms, and another group with certain symptoms of what is called angina pectoris. The infarcts in group 7 have been classified according to the appearance of angina pectoris in the after-course.

The distribution of the material may be seen from the table.

Results

The number of positive tests within each individual disease group seems to increase greatly according to the degree of clinical suspicion of the coronary heart disease.

When the whole material is distributed in the same way as the above-mentioned disease groups, the group where no (noteworthy) suspicion of a coronary heart disease occurs will have positive tests in 3 per cent of the cases, the group with suspected coronary heart disease will have positive tests in 20 per cent, and the group with probable or certain coronary heart disease in 30 per cent. When the cases which revealed coronary cardiographic changes already at rest are excluded from the calculation, the "exposing" hypoxæmia tests are obtained where the corresponding percentages equal 2, 18, and 23.

The cases with a pathological effect (positive tests) within the group with coronary curve at rest * will analogously amount to 4, 27, and 40 per cent.

The four cases in which the test turned out to be positive without any suspicion of a coronary heart disease comprised a man of 56 years with pulmonary emphysema and chronic bronchitis, a woman of 36 years with recently alleviated acute myocarditis and 2 women of 53 and 57 years respectively, with hypertension but no symptoms of angina.

Only 5 of the 18 cases with earlier infarction gave positive tests, all of which were still suffering from angina, while 13 cases gave negative or doubtful tests (the latter in 3 instances), 11 with and 2 without angina pectoris.

Seventeen of the 166 men disclosed positive tests, the corresponding figures for the women being 27 out of 160. The percentage distribution of male and female positive tests within the three main groups is, in group I, 1 and 5 respectively, in group II, 14 and 23 respectively, and in group III, 28 and 36 respectively.

When the total material is distributed according to age, the group under 30 years offers 16 per cent of cases with positive tests, the remaining groups being as follows: between 31–40 years 15 per cent, between 41–50 years 7 per cent, between 51–60 years 18 per cent, between 61–70 years 11 per cent, and above 70 years 23 per cent. It is remarkable that 7 cases out of 43 have had positive tests under the age of 30. They comprise a man of 29 years with hypercholesterinæmia and infarction later in the course of the disease, a woman of 16, and one of 21 years shortly after an acute myocarditis, 2 women of 22 and 27 years, respectively, with paroxysmal tachycardia, a woman of 22 without definite diagnosis (high sedimentation rate (Westergren)), and a woman of 24 with exogenous psychosis and sensations of fear.

When the material is distributed according to professions, a distinction being made between heavy and less heavy work, and a more indefinite group of housework, the percentage figure of positive tests will be 10, 13, and 17 per cent respectively.

When an enlargement of the heart is considered to occur, i.e. when the radiological volume of the heart exceeds 500 c.c./m.^{2} of body surface, among 18 cases with an enlarged heart in group I none had a positive hypoxæmia test, while 4 among 13 cases were positive in group II, i.e. 31 per cent. This also applies to 4 out of 8 cases in group III, i.e. 50 per cent. The corresponding figures, with regard to the cases with hearts of normal size in the several groups, were 3, 20, and 23 per cent respectively.

As regards cases with pulmonary disease and probably diminished pulmonary function, 1 out of 8 in group I and 1 out of 6 in group II had positive hypoxæmia tests.

* It is, of course, sometimes difficult to distinguish between coronary curves and those affected by digitalis. Eleven of the cardiograms denoted as coronary have been performed at a time when the patient had been given digitalis. It is doubtful in 4 cases whether earlier digitalis medication has as yet left any signs in the cardiograms. Thus, a possibility of digitalis influence has occurred only in 1 of the positive tests, 3 of the doubtful ones, and in 7 of the negative ones. Therefore, broadly speaking after considering the cases involved, a digitalis influence may be said not to be of any statistical significance in this material. When occurring, it must involve a slight increase in the percentage of positive tests at coronary cardiograms as compared with the figures stated above.

As already mentioned, 15 cases showed a decrease in the heart frequency after the test. Another 14, one of which later became positive, obtained a cardiographic improvement of the curve as compared with the cardiogram at rest.

So far 12 patients have been reported to have died. Two of them gave positive tests. One was found at autopsy to have a considerable coronary sclerosis as well as recent thrombosis. The other was not subjected to autopsy but had died within an hour in an anginal attack. One case with a doubtful test revealed at autopsy much dilatation of the right half of the heart but no coronary sclerosis. Two out of 8 cases with negative tests had coronary cardiograms at rest, unaffected by the test. One of them was examined post-mortem and showed extremely narrowed coronary vessels, the other died of an infarct 4 months after the test. Two cases had " cardiosclerotic " curve at rest. One of them showed, at autopsy, hypertrophy and dilatation of the heart, as well as moderate coronary sclerosis. The other died suddenly on the operation table after finished surgical intervention. No autopsy was performed. One patient with a normal cardiogram at rest had very slight coronary sclerosis and was considered to have died of an Adams-Stokes attack. Two have died of decompensated mitral valve disease. One was examined post-mortem and revealed a typical mitral heart but no narrowing of the coronary vessels. One patient died of pulmonary carcinoma and was not subjected to autopsy. Finally, one patient died at home 13 days after the test; he had earlier had an infarct and suffered such severe pains at the test as to necessitate its interruption without any registration of the curve: as far as is known, no autopsy was performed.

A positive test has later become negative in 4 instances. This has happened in the following cases: a man of 52 years with Bürger's disease, and another man of 67 years with certain angina pectoris, possibly with earlier infarction, who died later of a second infarct, as well as 2 women of 22 years of age, one with paroxysmal tachycardia and the other with no definite diagnosis. In the latter case the test improved parallel to the sedimentation rate and the clinical picture.

Exertion tests have been carried out in not quite a third of the number of cases, usually at the same pace as has been endured by the patient at the function test according to Nylin. These tests have often seemed difficult to judge on account of the tachycardia. When the tests, in which one S–T segment has been lowered to 1 mm. or more, or a T wave has been inverted (probably a very liberal interpretation) are regarded as positive tests, 16 out of 98 have turned out positive. The exertion cardiogram has been positive in 11 cases, while the hypoxæmia test has been negative, the condition being reversed in two instances. These figures do not, as yet, permit the drawing of any conclusions. However, it is possible that the hypoxæmia test and the exertion test affect the myocardium in different ways.

Discussion

Larsen's investigations have been performed on the basis of a different method. Levy *et al.* have, in their clinical classification, also taken into account the appearance of the cardiogram at rest. My figures cannot, therefore, be directly comparable to those obtained by them. However, the figure 20 per cent of positive tests for the whole of group II should correspond approximately to Levy's 18 per cent. Further, the figure 40 per cent in my material should answer to Levy's 55 per cent of positive tests at coronary sclerosis with angina and an abnormal cardiogram.

Finally, the question arises whether the results will repay the extra work and risks entailed in the method. The answer, of course, partly depends on the importance attached to the prognostic value of the positive hypoxæmia test. Is the artificial electrocardiographic coronary insufficiency, which may be in some cases brought about, a manifestation of a deteriorated coronary circulation and reserve even under physiological conditions? Levy describes a positive case where the autopsy revealed coronary sclerosis, and another case where death ensued owing to an infarct. The same applies in our material to the two positive cases where death has been reported. So far the material has been too restricted for critical conclusions but does, nevertheless, offer some indications. Also the question remains open whether it is less dangerous for a patient with angina pectoris to have a negative test than a

positive one. For the time being, care is advised in drawing conclusions from negative tests. In my opinion, the test has much to offer, for the diagnostic methods hitherto employed in this disease are inadequate and in urgent need of effective additions.

Finally, attention should be directed to future potentialities. The hypoxæmia test appears to " expose " several coronary cases which escaped notice at the simple cardiogram at rest. The same may apply, nevertheless, also to one or two cases which are not coronary in the actual sense. Still other coronary cases may escape notice at the hypoxæmia test. What is the reason for the varying outcome of the test? What factors play a part in this respect at the exchange of gas in the lungs, the heart and, perhaps, also in the central nervous system? The question may be asked, whether a local or general occurrence of the anatomical or functional insufficiency determines the electrical manifestation of the myocardial reaction towards the hypoxæmia stimulation. Such problems and many others in addition remain to be solved. The answer must be the outcome of various contributions from animal experiments, studies of autopsy material, and modifications and improvements of the technique. The latter refers, *inter alia*, to the discovery of the most suitable oxygen pressure in the gas mixture and control of the arterial oxygen saturation and the pH of the blood during the tests (which is certainly not the same in different patients according, i.e., to their technique of breathing).

Summary and Conclusions

After a brief retrospect of earlier examinations, a report is given of the particular technique used in hypoxæmia tests at the Sabbatsberg Sjukhus. The results obtained from 350 tests on 326 patients during the period 1942–44 are demonstrated. The number of positive tests is found to increase pronouncedly in accordance with the degree of clinical suspicion of a coronary heart disease. Thus, positive tests occur in only 3 per cent in the group without a suspected coronary disease, the percentage in the group with suspected coronary disease being 20, and in the group with probable or certain coronary disease 30. The material has also been analysed in several other important aspects. Finally, various possibilities for improving this part of the coronary diagnosis are discussed.

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MYXŒDEMA WITH PERICARDIAL EFFUSION

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Received September 14, 1945

There are few diseases that are so frequently mistaken in general practice as diseases of the thyroid gland. This not only applies to mild cases of thyrotoxicosis (Linnell, 1945) but also to cases of hypothyroidism and quite often even to fully developed cases of myxœdema with all its typical signs.

Just as in hyperthyroidism, in which the cardiac changes may be astonishingly small, there are instances of profound hypothyroidism with normal circulatory findings. Usually, however, the heart appears dilated to the right and to the left, and the cardiac sounds are muffled and soft. The term myxœdema heart has been applied to a condition found in about three-quarters of the cases of myxœdema (Zondek, 1918 and 1919; Fahr, 1925, 1927, and 1932; and Fournier, 1942). The myxœdema heart was described in the original report of Zondek (1918) in which he spoke of it as a clinical entity. Similar reports by Fahr, Fournier, and others, followed. Christian, and other observers, questioned the existence of such an entity and the cardiac signs were described as congestive heart failure complicating the myxœdema. It has, however, been proved that while digitalis is ineffective in those cases, treatment with adequate doses of thyroid is usually followed by a striking decrease of the size of the heart (reversible or "accordion heart"). Freeman (1934) and others found that at least part of the cardiac enlargement is due to pericardial effusion. White (1944) prints the picture of such a myxœdema heart in his text-book, showing a decrease of the transverse diameter of the heart shadow by 6 cm. as the result of successful treatment by thyroid. Considerable decrease in the size of the heart after thyroid treatment was further reported by Lehrman, Clark, and Means (1933) and by Campbell and Suzman (1934).

Cardiac involvement of a significant degree is an important sign, for it means that the grade of myxœdema is a serious one, or that other heart trouble, such as coronary or hypertensive disease, is present (White, 1944). Fahr (1925) found evidence of heart failure in 75 per cent of all his cases of myxœdema, 30 per cent of them showing rather severe signs and symptoms. While thyroid treatment relieved the signs and symptoms rather promptly, digitalis was found to be of doubtful value. He found many cases of myxœdema heart complicated by arteriosclerosis of the coronary vessels, and thyroid was found to be contra-indicated because the coronary flow may decrease at the same time as the power of the heart increases. The elevation of metabolism by thyroid therapy may induce symptoms of coronary insufficiency and attacks of angina pectoris may develop (White, 1944). In that case it is recommended to discontinue, or at least to reduce, the dosage of thyroid. According to White, congestive failure as a cause of death in myxœdema is very rare. The exact cause of the cardiac enlargement responsible for the term myxœdema heart is still a matter of dispute. It was thought to be the result partly of dilatation, partly of myxœdematous swelling and permeation of the myocardium by œdema, comparable to the alteration of the skin, and sometimes of an excess of fluid in the pericardium. While all these factors seem to play a role in the development of the myxœdema heart, recent observations seem to indicate that a pericardial effusion is generally present. Clear evidence of this was found in the case under discussion where a diagnostic paracentesis of the pericardial cavity revealed a pericardial effusion and 60 c.c. of straw-coloured fluid were aspirated. Similar results have lately been reported by a number of American observers but whether or not this effusion alone is responsible for all clinical signs is still uncertain. Tatum (1912) found pericardial effusion in thyroidectomised animals and Goldberg (1927) performed thyroidectomies on sheep and goats.

Two years later at autopsy he found the presence of pericardial effusion. The heart was pale and flabby and sections showed disintegration of heart muscle fibres.

Another interesting observation in myxœdema, and particularly in myxœdema heart with pericardial effusion, is the typical change of the cardiogram and the return of the tracing to normal after thyroid administration. In myxœdema the cardiogram is often characterized by an extremely low voltage curve. All the deflections are very small and inversion or absence of the T wave is not rarely found. Cutaneous alterations were at one time thought to be responsible for these changes. Recent investigations, however, tend to refute this assumption. Hallock (1933, 1934) found no abnormality in cardiograms of cases of generalized scleroderma and generalized ichthyosis. According to other observers the abnormal cardiogram and the cardiac enlargement of myxœdema results from myxœdematous swelling of the myocardial fibres. Adequate treatment with thyroid is usually followed by a striking improvement of the cardiogram. This too, was proved in the case under discussion. Since a reduction in the size of all waves of the cardiogram (low voltage) with occasionally inverted T wave in all leads is often found with effusion in the pericardial cavity, it may be difficult, if not impossible, to decide in a case of myxœdema heart whether the abnormal tracing is due to the myxœdema *per se*, or perhaps to a co-existing pericardial effusion. The alterations of the cardiogram in pericardial effusion are ascribed to the short circuiting of the action currents by the mantle of liquid which surrounds the heart so that only small potentials are intercepted at the surface of the body. The same alterations can be experimentally produced by the injection of normal salt solution into the pericardial cavity; such an artificial effusion can only be very small since a normal pericardium cannot be stretched. The low voltage tracing vanishes when the effusion is removed by therapeutic measures (Scherf and Boyd, 1945). To be sure the changes in the cardiogram in pericardial effusion are not invariably found, as in some cases the heart may not be entirely surrounded by fluid, and in some areas the heart may be adherent to the pericardium and to the surrounding tissues. An interesting cardiographic distinction between massive pericardial effusion and marked cardiac enlargement without effusion, has recently been suggested by Tung (1941): the duration of the electric systole (Q–T interval) is normal in the former and prolonged in the latter (White, 1944).

FIG. 1.—Teleradiograms of the heart before and after treatment.
(A) Before treatment, maximum transverse diameter 20·6 cm. (B) After treatment, maximum transverse diameter 12·0 cm.

Since no positive histological evidence proving the existence of a myxœdematous alteration of the myocardium has been obtained so far, the similarity of the cardiograms in pericardial effusion and in myxœdema could find its explanation in an abnormality common to both, that is, the effusion. It is therefore possible that a pericardial effusion existed in many, perhaps in all cases described under the term myxœdema heart.

Case Report

Miss A., aged 30 years, was admitted to hospital in January, 1945. For the last six months she had complained of dyspnœa on slight exertion, swelling of the ankles, puffiness of the face with swelling under the eyes, clumsiness of the hands, and loss of energy. She had put on a considerable amount of weight during the last few months and it was noticed that her speech became slow and slurred, although the patient herself was not aware of this.

On examination the temperature was subnormal, the respiration rate 20, and the weight 10 stone. Sallow pallor of skin which was dry and scaly, particularly on arms and legs, cyanosis over malar prominences, dry and brittle hair with some loss of outer third of eyebrows, puffy eyelids with narrow lid-slits, forehead slightly wrinkled, voice hoarse, speech slow and slurred, slow reactions, and slightly retarded cerebration. Cardiac dullness greatly increased to right and left. Cardiac impulse not visible. Apex beat displaced outwards and downwards, as judged by the intensity of the heart sounds, within the area of cardiac dullness. Heart sounds soft and distant, no thrill nor murmurs. Pulse 60 a minute, small, regular, and equal. Blood pressure 105/70. Abdomen rather prominent and flabby, but no evidence of fluid made out. Nothing abnormal palpable. No œdema.

The diagnosis of myxœdema with myxœdema heart was made.

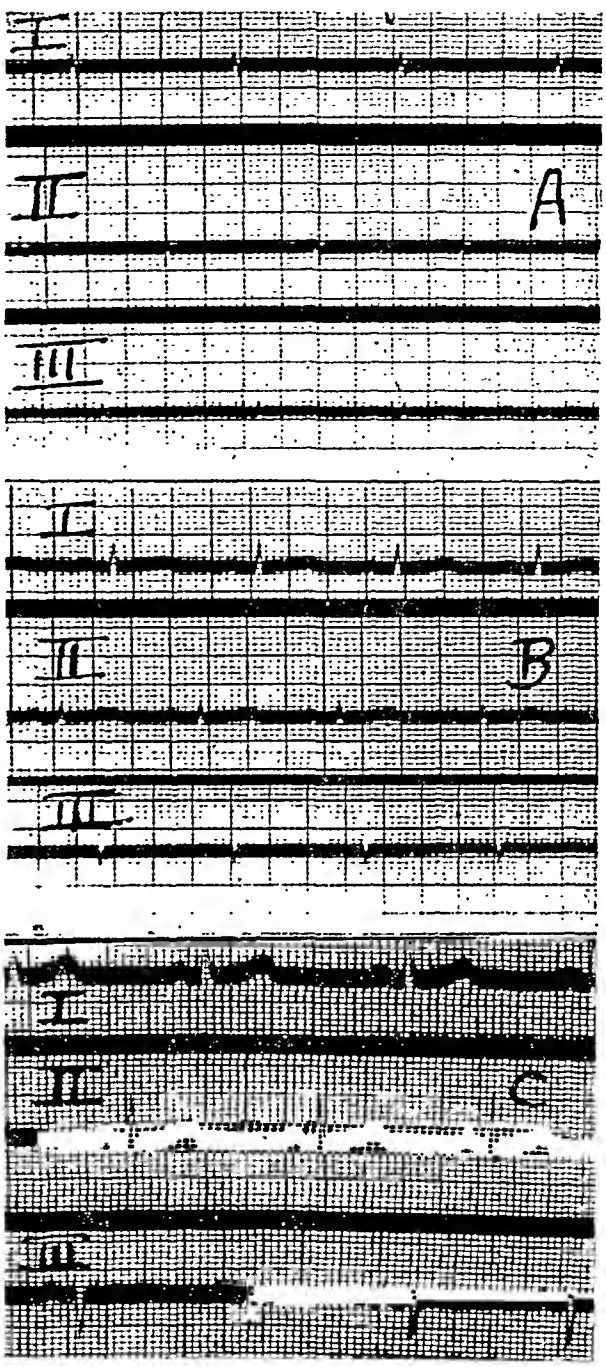

Fig. 2.—Electrocardiograms before and after treatment. (A) On admission, with extremely low voltage of all excursions. (B) After two months treatment with thyroid, showing increasing, but still low, voltage. (C) On discharge, showing return to normal, with left axis deviation.

X-Ray of heart on admission showed gross cardiac enlargement to the right and to the left, the maximum transverse diameter being 20·6 cm. (Fig. 1A). The electrocardiogram showed a low voltage curve and complete absence of P and T wave in all leads (Fig. 2A). Paracentesis of the pericardial cavity revealed the presence of a pericardial effusion. The needle was inserted in the fifth left intercostal space four and a half inches from the sternal border, and 60 c.c. of clear, straw-coloured fluid were aspirated. Plasma cholesterol 305 mg. per 100 c.c. Hæmoglobin 64 per cent. Red blood cells 3,230,000 per cub. mm. Colour index 0·98. White blood cells 5700 per cub. mm. Erythrocyte sedimentation rate 38 mm. in 1 hour (Westergren). Wassermann negative. The basal metabolic rate was not estimated

as no apparatus was available and the progress of the case was ascertained by monthly estimations of the plasma cholesterol.

Treatment and Progress. A trial dosage of thyroid, ½ grain b.i.d., was given for a week. It was then increased to 1 grain t.i.d., as no unfavourable reactions were observed. On this dosage the patient was kept for the next ten weeks when thyroid was reduced to ½ grain b.i.d. as a maintenance dose. She was also having fersolate tablets.

A series of radiograms of the heart showed a steady decrease in the size and the final one, after four and a half months of treatment with thyroid, showed a total decrease of the transverse diameter of the heart shadow by 8·6 cm. (Fig. 1B). The electrocardiogram became normal with all deflections well defined (Fig. 2 B and C), but there was now evidence of left ventricular preponderance. Blood pressure 120/85. Plasma cholesterol 185 mg. per 100 c.c. Hæmoglobin 94 per cent. Erythrocytes sedimentation rate 10 mm. in 1 hour. The raised erythrocyte sedimentation rate before treatment was probably due to the associated anæmia.

The patient was extremely fit on discharge, all the signs and symptoms of myxœdema had subsided, and she had lost 22 pounds within three months. She was advised to continue with the maintenance dose of ½ grain of thyroid, twice a day.

Summary and Conclusions

Some of the reported cases of pericardial effusion in myxœdema heart are reviewed, and the typical changes in the size of the heart and in the cardiogram are discussed.

A case of advanced myxœdema with gross enlargement of the heart in a woman of 30 years of age is recorded. Pericardial paracentesis revealed a pericardial effusion. The transverse diameter of the heart shadow before treatment was 20·6 cm. and after four and a half months of treatment with thyroid it decreased to 12 cm., showing a total decrease of 8·6 cm.

An initial low voltage curve of the cardiogram with absence of T wave in all limb leads was restored to normal after treatment, but there was evidence of left ventricular preponderance.

A trial dose of thyroid, ½ grain b.i.d., was given and as no unfavourable effect was observed this dose was increased to 1 grain t.i.d., and was finally reduced to ½ grain b.i.d. as the maintenance dose.

The similarity of the electrocardiograms in cases of pericardial effusion and in cases of myxœdema, suggests a common abnormality which may be the presence of fluid in both disorders. This would then support the opinion that a pericardial effusion exists in many, if not in all cases described as myxœdema heart.

We have to thank Dr. P. J. W. Mills, Medical Superintendent, for his kind permission to publish this case, and Dr. John Parkinson and Dr. J. W. Linnell for their interest and encouragement in the preparation of this paper. Our thanks are also due to Dr. Cornelius Papp for supplying us with some of the references, and to Dr. Cedric Hilliard, Radiologist, and his technical staff for their kind co-operation.

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ANGINA PECTORIS WITH ASSOCIATED LEFT PAROXYSMAL PTOSIS

BY

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Received October 12, 1945

The present case is reported because it presents what appears to be a unique combination of clinical phenomena.

An officer, 48 years of age, was well until August 1943. At this time, and at the end of a strenuous ten-day battle course, he was climbing a high wall when he had a sudden attack of severe pain in the chest accompanied by breathlessness. The pain did not radiate, but was generalized over the sternum and all the ribs on the left side anteriorly. He felt as though his chest was gripped in a vice and was very badly shaken, and stayed in bed for two days. A few days later he was " dressing down " one of his subordinates and at the same time vigorously demonstrating how a job should be done, when he suddenly felt an intense pain in the xiphisternum accompanied by severe dyspnoea. He had to stop talking and sit down at once and the pain slowly disappeared during the course of the next ninety minutes. At 3.30 the next morning he was awakened by a severe pain in the left arm, beginning in the elbow and spreading down the dorsum of the arm to all the knuckles; it was particularly acute in the thenar muscles. At the same time he became aware, though less insistently, of a mid-sternal pain, but on this occasion the arm pain was the more severe and was described as being like electric shocks passing down the forearm in rapid succession, rendering the hand practically powerless. He slept no more that morning but by breakfast time the pain was gone except for a dull ache in forearm and sternum. From this time until mid-December he had constant aching discomfort in the chest and left arm which turned to severe pain on moderate exertion. The continual pain in the arm was not well localized except that it was all below the elbow. Exertion, however, produced well-defined pain and tingling in the ulnar forearm and fingers, and if the exertion was continued the pain spread to the radial side of the hand and to the thenar muscles.

One day in October he was cycling uphill and already feeling rather breathless when he suddenly became aware that his left eye was running and that tears were streaming down his face on this side. He attributed this to the cold wind, and when he dismounted his bicycle, five minutes later, there was a burning pain on the left side of his face affecting chiefly the temple, eye, cheek, and angle of the lower jaw. At the same time he noticed that his left face felt warm and sticky. He lectured for nearly an hour in this condition and was then suddenly seized by a severe pain, which was mid-sternal and involved the whole of the left forearm and hand simultaneously. This was as severe as any attack he had ever suffered, but it disappeared after half an hour's rest and within an hour his eye had stopped running.

From this time on all the severe attacks began in the same way, with watering of the left eye followed by pain in the left face which was observed to be warm, congested, and moist to the touch. He noticed that if he sat down at the onset of lachrymation the subsequent chest pain was either much less severe or, on some occasions, did not come on at all; and that the onset of attacks with running of the left eye bore a constant relation to exertion, occurring always during the same hundred yards of his uphill journey from his place of work. If he exerted himself severely indoors the eyes watered in the same way, though, of course, he was

more commonly outside when this happened. When the exertion was violent and sudden, as in cycling up a steep hill against the wind, and particularly after lunch, the chest and arm pain sometimes occurred immediately, without lachrymation or facial pain, but on those occasions the latter symptoms began a few moments later and usually together.

He continued thus until mid-December. One afternoon just as he was recovering from an attack of post-prandial exertional pain he had his photograph taken. When the picture came back from the printers, he noticed that his left eye was practically closed. This was the first occasion on which ptosis was noted, and after this time he observed a gradual drooping of the left lid simultaneously with the onset of the other ocular symptoms in every attack. The ptosis was such that in a severe attack he could not see except by raising the lid manually.

In mid-December the constant chest and arm pain cleared, but he still had frequent exertional attacks of the same type and severity as before. They began with weeping and pain in the periphery of the left face and with flickering in the upper and lower lids, after which the upper lid began to droop. Usually about half an hour later pain began simultaneously in the chest and arm. This period was inversely proportional to the severity of the provoking exertion, and again, if this was severe and sudden, the related facial and ocular phenomena would follow the onset of angina. The eyelid remained down for the whole day following an attack, but on waking the next morning the lid was normal or showed only slightly ptosis; the same result often followed a short sleep even in the afternoon after an attack. Ptosis occurred with all severe attacks and he began to use it as a signal that, unless he rested, severe pain would certainly follow.

He never had any double vision or impairment of vision during these attacks, until on one occasion the day after a severe attack he noticed persistent diplopia on looking upwards. Sweating of the left side of the face during attacks became increasingly prominent.

When he inhaled amyl nitrite the chest and arm pain gradually disappeared over a period of time up to about fifteen minutes, depending on their severity. The pain in the face disappeared simultaneously, but the drug had no effect on the weeping or the ptosis, the former lasting for about half to one hour after the pain cleared and the ptosis until next day, or at any rate until after a period of sleep. Careful enquiry showed that the weeping and ptosis was always accompanied by mild mid-sternal discomfort and dyspnoea, and always followed by facial pain and then by chest and arm pain unless he rested absolutely at the onset.

The patient was admitted under our care on July 16, 1945, and has remained under observation for three months. Physical examination on admission showed an obese subject with a pulse rate ranging between 60 and 80 a minute and a regular rhythm. The brachial vessels were thickened, but the heart size and sounds were normal and no murmurs were heard. The chest and abdomen showed no signs of disease and the nervous system was intact. No cranial bruits were heard. The blood pressure was 140/80, and the urine showed no abnormal constituents. Radiological examination showed no evidence of cardiac or aortic enlargement and there was no peripheral arterial calcification. The Wasserman reaction was negative. Cardiography showed left axis deviation and steep inversion of T III.

Three attacks were observed before relief was obtained with vasodilators: in symptomatology they were identical with those described by the patient. The following observations were made during the half-hour preceding the onset of chest pain. The pulse rate showed no change but the blood pressure rose to 170/110. There was flushing of the whole of the left face with hyperhydrosis, extreme conjunctival congestion, left pupillo-dilatation with retention of normal pupillary reactions (evident only in a dim light and therefore sympatheticotonic), striking dilatation of the retinal veins on ophthalmoscopy, and left ptosis of moderate degree and gradual onset. Electrocardiography during an attack showed inversion of T II in addition to the previous findings. The facial and ocular symptoms cleared within an hour of relief of the pain by amyl nitrite inhalation, except that the ptosis remained: next morning the ptosis was still evident though less. After the second and severest attack it persisted for four days and was associated with vertical diplopia. At this stage he was seen by Squadron-Leader R. S. Sampson, ophthalmologist, who reported left ptosis and weakness of the left superior rectus muscle as revealed by red-green glasses and the Maddox rod test. At the same time conjunctival instillation of one drop of 1/1000 adrenalin, carried out at his suggestion, revealed left sympatheticotonia as shown by left pupillo-dilatation, the right pupil being unaffected.

Radiological examination of the skull, including stereoscopic views of the pituitary region and the sphenoidal fissures showed no deviations from normal and in particular no abnormal calcification or vascular shadows.

At present (10/10/45), after prolonged rest in bed, he is free from symptoms except for occasional post-prandial and exertional dyspnoea, usually preceded by left lachrymation and conjunctival suffusion.

Discussion

The phenomena described above as preceding and accompanying the patient's attacks of angina pectoris are not easy to explain. The features shown in the face and eye appear to comprise two clearly defined components. First, there is evidence of irritation of the cervical sympathetic in lachrymation, hyperhydrosis, vasodilatation, pupillo-dilatation, and abnormal pupillary response to adrenalin. Secondly, there is evidence of a partial paralytic lesion of the third cranial nerve, in ptosis and paresis of the superior rectus muscle, producing diplopia.

Wide irradiation of different impulses in the spinal cord might be related to the first group of symptoms, but would not explain the second. Of intermittent pressure from a dilated or aneurysmal vessel within the skull the reverse is true. Yet the constant association and close time-relation of the two components of the syndrome indicate the probability of an equally close relation in their mode of production.

Consideration of the anatomical pathways involved suggests a possible resolution of this difficulty. The nervous pathways of cardiac pain are not completely understood, but are considered to pass mainly via the sympathetic afferents of the cardiac plexus to the middle and inferior cervical (stellate) ganglia and the cervical sympathetic chain. From here they pass into the cord by way of the white rami communicantes and the upper four thoracic and possibly the eighth cervical posterior roots, to terminate at the base of the posterior horn in relation to the origin of the spino-thalamic tract.

The sympathetic pupillo-dilator fibres originate in cells of the posterior hypothalamic nuclei, having connections there with cortical levels, and they pass down through the medulla and cervical spinal cord in close relation with the pyramidal tracts, to terminate in the cilio-spinal centre, situated in the lateral horn of grey matter at the levels of the eighth cervical to the second thoracic segments. Here, preganglionic fibres originate, and, passing out with the lowest cervical and upper two thoracic anterior roots, make their way via the white rami communicantes to the inferior cervical (stellate) ganglia. These fibres course up the sympathetic chain to their cell-station in the superior cervical ganglia, where post-ganglionic fibres arise to be distributed to the eye by way of the coat of the internal carotid arteries and their branches. The sympathetic supply to the other parts concerned in Horner's syndrome—the tarsal muscles, the muscle of Muller, and the facial sweat glands and blood vessels—follow a similar, if less clearly defined, route.

These two pathways, the one afferent and the other efferent, therefore have part of their course (between the stellate ganglion and the spinal cord) in common, except that the bulk of the afferent fibres probably pass in the posterior, and the bulk of the efferent fibres in the anterior roots of the same segments. More significantly, their cell-stations within the spinal cord are in close proximity. The cilio-spinal centre lies in the lateral horn of the grey matter between the eighth cervical and second thoracic segments, with the related sympathetic efferent cell-stations close by, while the synaptic connections between the cardiac visceral afferents and the cells of origin of the spino-thalamic tract lie at the base of the posterior horns at the same levels of the cord.

These anatomical considerations suggest that the sympathetic symptoms in the present case are produced in the spinal cord. MacKenzie's hypothesis of segmental and extra-segmental sensory irradiation is used to explain the wide somatic reference of anginal pain, which in this case involved all dermatomes from the third cervical to the first thoracic, and it is perhaps significant that the facial pain in the present case also indicates a very widespread irradiation. The peripheral site of this pain, affecting chiefly the temple, cheek, and jaw, and sparing the nose and the central parts of the face, suggests a central origin and is consonant with excitation of the lower part of the sensory nucleus of the fifth nerve which extends

into the cord as far as the second cervical segment. It is known that referred cardiac pain may be accompanied by, and on occasion replaced by, sweating in the area of reference, while the salivation and polyuria that occasionally accompany angina pectoris can hardly be explained otherwise than as viscero-sensory reflexes similarly excited by irradiation from cardiac afferents.

In the present case, therefore, it is suggested that the sympatheticotonic phenomena were due to central irradiation within the spinal cord. The nature of the recurrent partial paresis of the oculo-motor nerve indicates a peripheral lesion, recoverable and probably involving only the superior ramus of the nerve that supplies the two muscles involved (levator palpebrae superioris and superior rectus). The delayed onset and slow recovery of the third nerve signs supports a mechanical causation, and we suggest that the paresis may have been due to local pressure on the superior ramus of the nerve by a dilated artery. The anterior site of the third nerve involvement, and the failure to elicit any evidence of impaired function in the first division of the fifth nerve on repeated testing during and between attacks, suggests that the ophthalmic artery or one of its branches rather than the internal carotid was responsible, and in its distension both the widespread sympathetic vasodilatation and the pre-anginal rise in blood pressure may have played a part.

Conclusions

A case of angina pectoris with two unusual groups of associated symptoms is described. In the first there was evidence of irritation of the cervical sympathetic, as shown by lachrymation, hyperhydrosis, vasodilatation, pupillo-dilatation, and an abnormal pupillary response to adrenalin. In the second there was evidence of a partial paralytic lesion of the third cranial nerve resulting in ptosis and paresis of the superior rectus muscle, producing diplopia.

The possible mechanisms have been discussed. It is suggested that the sympathetico-tonic phenomena are due to central irradiation within the spinal cord and that the recurrent partial paresis of the oculo-motor nerve may be due to local pressure on the superior ramus by a dilated opthalmic artery.

We wish to thank Squadron Leader R. S. Sampson for many helpful suggestions in relation to this case.

INDUCED CHANGES IN THE CIRCULATION IN CONSTRICTIVE PERICARDITIS

BY

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Received September 21, 1945

It is accepted that constrictive pericarditis curtails the normal excursion of the ventricles. This leads to a diminution in the output of the heart per beat, and, in spite of an elevated pulse rate, to a diminution also in the output of the heart per minute. Nearly all the studies of the circulation in patients with pericardial obstruction (Beck and Griswold, 1930; Burwell and Strayhorn, 1932; Beck and Cushing, 1934; Maltby, 1934; Burwell and Flickinger, 1935; Burwell and Blalock, 1938; Stewart, Heuer, Deitrick, Crane, Watson, and Wheeler, 1938) have been carried out under standard or basal conditions. The purpose of this paper is to place on record some additional measurements of the circulation under standard conditions, and also to report a series of studies of patients with constrictive pericarditis made under various special circumstances. These special studies include observations of the changes in the circulation associated with alterations in the blood volume, the pulse rate, and the venous pressure.

Presentation of Patients

The observations were made during the study and treatment of two patients, now to be described.

Case 1. G. M. was born in 1900. In April 1931 he developed right-sided pleurisy with effusion. His rather mild disability disappeared after removal of the fluid by tapping, and for several months he considered himself well. In November 1931 he was found to have a left-sided pleural effusion. There was fever, and active tuberculosis of the left apex was demonstrated by X-ray. At about this time he first noticed that his ankles were swollen and that he became short of breath in climbing a short flight of stairs. Under sanatorium care he improved. In 1932 he had another period of fever, this time associated with swelling of the abdomen, and he entered the Peter Bent Brigham Hospital. Here he was found to be a slight young man, a little pallid, but with a bluish tinge to the nail beds. The area of cardiac dulness was enlarged, the heart rate rapid, and the sounds distant. No murmurs were heard. The arterial blood pressure was 124/60. The abdomen was distended by ascites, and the liver was felt 3 cm. below the costal margin. The fluoroscope revealed the signs of apical fibrosis of both lungs and a considerably enlarged cardiac shadow said to be of water-bottle shape. The amplitude of the cardiac excursion was described as good.

Abdominal paracentesis removed 1800 c.c. of fluid in which tubercle bacilli were demonstrated by guinea-pig inoculation. As fluid slowly reaccumulated he complained of præcordial discomfort and a sense of drawing and tightness under the sternum which was worse on inspiration. After four months he had shown no improvement. The arterial pressure had declined to 98/64, the liver was larger, and the veins more distended. Fluoroscopic examination revealed the heart shadow to be no longer enlarged, and the amplitude of the cardiac excursion was now described as poor.

He went back to the sanatorium and after some months of rest in bed was much better. He was then permitted graded activity and in April 1934 was discharged.

From April 1934 until resection of the pericardium in 1938, his condition changed but little. He

was comfortable at rest but suffered dyspnœa and weakness on exertion, even such slight exertion as walking on the level at the usual pace. This severe limitation of exercise tolerance prevented him from performing the manual labour on which his livelihood depended.

Our own observations began in December 1935, and we have been in touch with him ever since. On any visit before the operation of 1938 he would display the following physical signs: the face was full and *suffused;* the feet and hands were cold to the touch and often clammy; there was a little cyanosis of the nail beds and an exaggerated longitudinal curvature of the nails. The neck veins were distended and firm and the venous pressure (see later) was always above the normal limits. The cardiac dulness was no longer as large as it had been, but measured only 4·5 cm. to the right and 6·5 cm. to the left. The dulness did not shift with change in the patient's position. The heart rate was more rapid than normal, the rhythm was regular, the sounds faint, and there were no murmurs nor additional heart sounds. The arterial pressure was 108/90 and there was slight paradoxical fluctuation. The lungs (in which there were changes consistent with healed fibrous tuberculosis) showed no moist rales. The vital capacity was moderately reduced (usually it was about 2400 c.c.). The liver was usually to be felt 3 or 4 cm. below the rib margin. Ascites was not present at this time.

It was apparent that we were dealing with constrictive pericarditis, the cause of which was tuberculosis and the result of which was an obstruction to blood flow of only moderate degree. (This will be shown clearly in the measurements reported later). Because his symptoms were mild and apparently non-progressive, operation was not then advised. Instead he was given graded exercise in an attempt to improve his general condition. He followed the regime faithfully but over the years seemed, if anything, to lose ground rather than to gain it. His limitations, although slight, were disabling, and in 1938 it was decided to advise treatment by operation.

On February 10, 1938, under avertin-ether anæsthesia, Dr. E. C. Cutler performed a pericardiolysis. At operation an interesting situation was found which was described in the operative note as follows: "When the pleura on the left was pushed aside it was noted that in the lower portion of the field there was a vigorous ventricular contraction while the upper portion of the field was motionless and muscular contraction was palpated as if through a thick sheet. The pericardium was opened and freed from the heart muscle down to the phrenic nerve on the left and to the right into a stiff area of diseased tissue. This area led into broken-down cheesy material quite characteristic of tuberculosis of the pericardium. Directly under the pericardium on the upper portion of the right ventricle lay a sheet of very hard fibrous tissue which limited the muscular movements beneath it. This *epicardial scar* was carefully shaved away and as it was removed there was marked improvement in the ventricular contraction, so much so that the muscle actually bulged into the field."

On microscopic examination the tissue removed was found to be dense hyalinized collagen with granulation tissue both old and recent. No tubercle bacilli were seen and no evidence of active tuberculosis was found. The pathologist's impression was that the tissue could be classified as healed tuberculous pericardium.

Almost immediately after the operation there was a change in the physical appearance of the patient. The suffused appearance of the face disappeared, the cyanosis of the nail beds was replaced by a normal pink colour, and the hands were no longer cold and clammy. At this time the venous pressure was within normal limits. After a fortnight, however, the pressure in the veins increased and it remained elevated for the next four months. During this time the patient experienced progressive gain in comfort though there was little laboratory evidence to suggest it. His ability to perform physical work improved, as did his sense of strength and well-being. Gradually, over months, his strength grew and his venous pressure fell. He became able to walk on the level without discomfort, climb hills or stairs without difficulty, and before long returned to his former occupation.

One more tuberculous chapter was written in his history in 1939 when he developed bone tuberculosis involving the right femur.

Since 1935 he has been under frequent observation in the laboratory. Many of the observations made there apply to the description of the course of his disease. They are reported in a subsequent section of this paper.

Case 2. (The course of this patient's illness has already been described by Burwell and Ayer (1941) in another connection; only a summary account will be presented here.) A. B. was a Lithuanian labourer of 54. In January 1938 he began to suffer from cough and coryza. A few weeks later he experienced dyspnœa on exertion, followed shortly by dyspnœa at rest, by orthopnœa, and by œdema of the ankles. When he entered the hospital on March 12, 1938, the heart rate was rapid, the rhythm regular, the pulse small. The heart was not enlarged and no murmurs were heard. The neck veins were visibly distended; the liver edge was 5 cm. below the rib margin; there were signs of fluid in both pleural cavities; and there was slight œdema of the ankles. A friction rub was audible over the præcordium and in the left axilla. The arterial blood pressure was 100/70 mm.; the venous blood pressure was 210 mm. of water. At fluoroscopic examination the excursion of the left heart border

was considered to be less than normal and there was *no* visible movement of the right border. An electrocardiogram showed low voltage, inverted T II and T III, and a normal lead IV.

Some improvement in comfort followed a few days of hospital care, during which time his chest was tapped and he received digitalis and mercurial diuretics. When he had lost some 16 pounds of fluid by various routes he could lie flat without dyspnœa and the vital capacity was found to be 3100 c.c., but the peripheral venous pressure remained elevated. The temperature rarely rose above 99° F. and was usually within limits considered normal.

A diagnosis of constrictive pericarditis was made. Tuberculosis was considered the cause of the pericarditis since the pleural fluid was found to contain tubercle bacilli by guinea-pig inoculation. Operation was advised. After nearly three months, during which time his disability continued and his venous pressure remained high, the patient decided to accept this advice. Dr. Cutler performed the operation in July 1938. He found a tough fibrous pericardium about 3 mm. thick closely applied to the heart. The entire anterior portion of this was excised and the heart was observed to pulsate more vigorously.

The venous pressure (Lyons, Kennedy, and Burwell, 1938) fluctuated somewhat during the first week after operation, but after that was never above 105 mm., i.e. it was well within normal limits. The evidences of congestion disappeared and it was considered that operation had relieved the mechanical obstruction to the entrance of blood into the heart. An account of his further course and of his tragic death from constrictive pleuritis a few weeks later has been recorded elsewhere (Burwell and Ayer, 1941).

These two patients, then, suffered from tuberculous pericarditis with constriction of the heart. Both had disability that was not extreme, and both were co-operative and interested participants in our studies of them. They were thus particularly suitable for the type of observation now to be described.

Methods of Study

Accepted methods were used for measuring various aspects of the circulation. The cardiac output was determined by the acetylene method, using the three-sample modification described by Gröllman, Friedman, Clark, and Harrison (1933). The venous pressure was measured by the direct method as applied by Lyons, Kennedy, and Burwell (1938). The blood volume was measured by the method of Gibson * and Evelyn (1938). Circulation time was the arm-to-tongue time indicated by the intravenous injection of 4–5 c.c. of sodium dehydrocholate.

Most of the observations on both patients were made while they were ambulatory. The patient would come to the laboratory in the fasting state, and after preliminary determinations of vital capacity he would rest in a reclining chair for 45 to 60 minutes before the estimation of the cardiac output was made. Following the determination of the cardiac output he was placed on an examining table for the measurement of venous pressure, circulation time, arterial blood pressure, and blood volume. When the patient did not have a determination of the cardiac output he rested on the examining table at least 15 minutes before the venous pressure was measured.

The observations made may be divided into two groups: those made under standard conditions before and after operation; and those made before, during, and after induced alterations in the circulation.

Observations Under Standard Conditions

Measurements of the venous pressure, blood volume, and cardiac output made under basal conditions before and after operation, are recorded in Table I and illustrated in Fig. 1 for Case 1, and recorded in Table II for Case 2. A persistently elevated venous pressure and a persistently low cardiac output per minute and per beat were present in both patients prior to operation. The blood volume in Case 1 was above the normal values. In Case 2 it was within the normal range based on height. It may be that the considerable emaciation and muscle atrophy in this patient affected the estimation of the normal values from his height or weight.

* We are indebted to Dr. J. G. Gibson II for his co-operation in making the measurements of the blood volume.

TABLE 1

OBSERVATIONS ON CASE 1

Date	Venous blood pressure, mm. water	Total blood volume in c.c.	Heart rate per minute	Oxygen consumption per minute	A-V difference vol. O_2 per liter blood	Cardiac output liters per minute	Systolic output in c.c. per stroke	Blood flow in liters per sq. m. surface area	Vital capacity in c.c.	Circulation time in seconds	Arterial blood pressure, mm. Hg.
Normal-values	Below 150	5400	64	231	59·0	3·87	60·4	2·21	4350	15–20	120/80
15/1/36	175	5870	81	242							
31/1/36	190		80	226							
28/2/36	175		80	210	61·1	3·44	43·0	1·99			
26/3/36	230		80	204	61·6	3·31	42·0	1·91	2350		112/80
2/4/36	180									39	
23/4/36	195									36	
21/5/36	202		70						2350	43	112/85
21/7/36	180								2500	35	114/74
16/12/36	217	6570	74	213	65·0	3·28	44·0	1·89		41	
2/3/37	211		80	221					2250	30	118/90
23/3/37			80						2500		
3/6/37			84						2200		108/82
22/7/37	230		76	215	65·0	3·30	43·4	1·93		44	104/76
5/8/37	223		72	201	66·0	3·00	44·6	1·72	2150		114/74
18/10/37	185								2500	30	
15/11/37	190	6125	72	218	65·0	3·36	46·6	1·93	2350	34	112/90
6/12/37	215										
15/1/38	195		72	211	68·7	3·07	40·4	1·74	2300	42	106/78
27/1/38	215	6560	74	229	68·5	3·34	45·1	1·94		42	
5/2/38	207		76							35	
10/2/38					Pericardiolysis						
15/2/38	115		80						1500	30	126/88
16/2/38	125								1650	30	112/70
18/2/38	125		80						1600	26	114/78
23/2/38	135	5400	90						1850	28	
26/2/38	150								1850	35	
1/3/38	140		80	203	55·7	3·64	45·5	2·26		32	
5/3/38	175		80	188	62·1	3·06	37·9	1·76	2100	30	110/82
9/3/38	170	5180							1900	28	
12/3/38	170		80	192	51·0	3·76	47·0	2·25	1900	45	112/82
15/3/38	210									50	
18/3/38	193	5910	76	198					2150	50	112/82
19/3/38			76	201	58·4	3·44	45·3	2·06			
31/3/38	185		76	211	66·8	3·16	41·5	1·93	2100	43	96/66
11/4/38	195		76	224	69·8	3·21	43·4	1·87		35	106/64
20/4/38	153									21	
26/4/38	190	6050	72	216	66·0	3·21	45·5	1·90	2200	25	
30/4/38	193		80							31	
16/5/38	155		72	251	65·9	3·81	54·4	2·22	2300	37	
27/5/38	170		70	210	59·8	3·51	50·2	2·03		39	
7/6/38	163		66	195	61·8	3·15	45·6	1·83	2400	40	
29/6/38	158	6040	72	210	68·6	3·06	42·5	1·79	2400	29	
21/9/38	125		72	208	68·0	3·06	42·5	1·79		32	
30/9/38	124	5650	66	205	67·0	3·06	46·0	1·79		22	
7/10/38	136		72						2550		112/70
1/2/39	115										
8/6/39	150	6040	66	203	59·5	3·41	51·6	1·98	2600	34	
30/3/40	110										
13/11/40	108	5300	70	196	51·5	3·83	53·2	2·06	2500		110/70
17/4/41	148		74	209	62·1	3·36	45·4	1·98			110/80
25/4/41	135		68								
26/5/42	125								2600	25	
24/4/43	135								2450	27	120/80
5/6/43			76	190	61·2	3·22	42·4	1·95			
5/4/44	126								2700		120/85

TABLE II

OBSERVATIONS ON CASE 2

Date	Venous blood pressure, mm. water	Total blood volume in c.c.	Heart rate per minute	Oxygen consumption per minute	A-V difference vol. O_2 per liter blood	Cardiac output liters per minute	Systolic output in c.c. per stroke	Blood flow in liters per sq. m. surface area	Vital capacity in c.c.	Circulation time in seconds	Arterial blood pressure, mm. Hg.
Normal values	150	5400	64	212	59·0	3·68	57·7	2·2	4250	15–20	120/80
21/3/38	255									19	100/70
28/3/38		5450	74	186	84·4	2·20	29·0	1·31	1800		
30/3/38	250		72	191	81·2	2·35	32·7	1·39		20	
1/4/38	237		72	197	84·9	2·32	32·2	1·37	1800	33	112/86
3/4/38					Digitalis stopped						
5/4/38	185*	5070*	70*	193*	78·5*	2·46*	34·6*	1·52*	1800*	26*	
12/4/38	232		72	175	74·0	2·35	32·7	1·42	1800	36	
14/4/38	245		76						1800	29	112/90
20/4/38			82	183	74·0	2·47	30·7	1·47			
21/4/38	213		78	176	74·0	2·40	30·6	1·46		18	
10/5/38	265†		100†	200†	78·0†	2·57†	25·7†	1·53†	1800†	33†	118/80†
24/5/38	205‡		88‡	163‡	62·0‡	2·64‡	30·0‡	1·57‡	2200‡	37‡	100/84‡
26/5/38	195§	4870§	88§	188§	74·0§	2·51§	27·9§	1·50§		38§	
14/6/38	208		88	189	84·0	2·24	26·0	1·33		39	
1/7/38	283‖		90‖							44‖	
8/7/38	265		88	197	75·0	2·63	30·0	1·56			
13/7/38					Pericardiolysis						
14/7/38	220		88								105/86
15/7/38	205		86								118/80
16/7/38	155		88								122/84
18/7/38	125		92								
20/7/38	110		94								130/90
28/7/38	122	4700									
8/8/38	150									18	
30/8/38	141									17	

* After mercupurin diuresis. † After high salt and unrestricted fluids.
‡ After 3 g. NH_4Cl daily and 2 mercupurin suppositories weekly.
§ After 2 c.c. mercupurin intravenously. ‖ Without diuretics or other drugs.

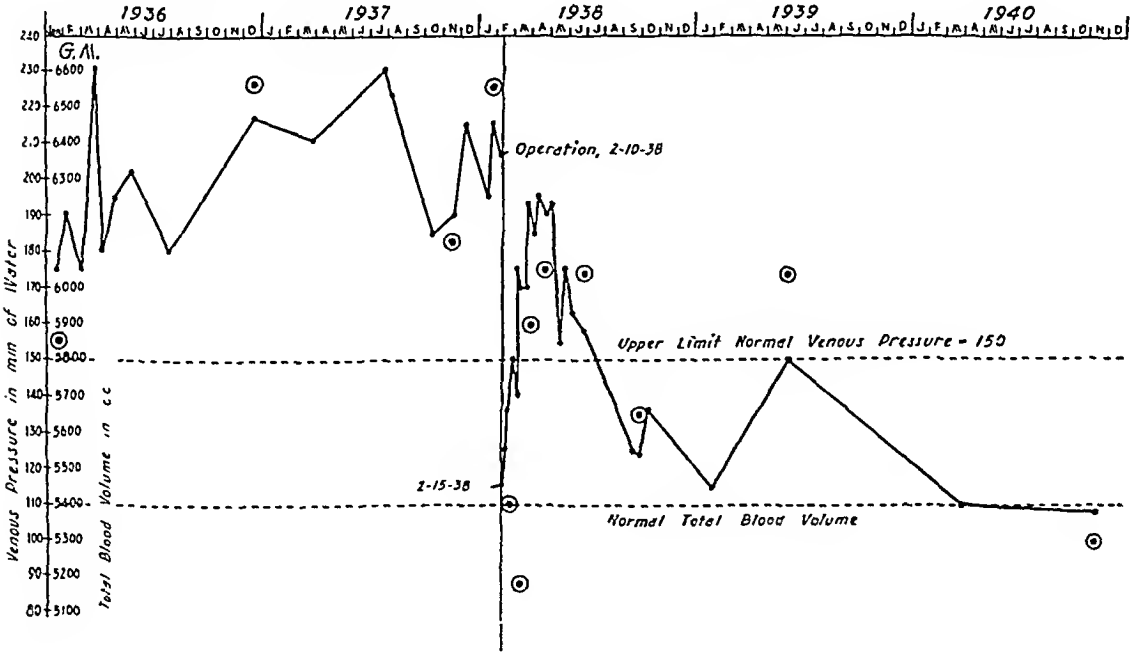

FIG. 1.—The course of the venous blood pressure and the total blood volume in Case 1 before and after pericardiolysis.

In both patients the venous pressure decreased after operation so that it was within the normal range. Of special interest was the *rise* in venous pressure two weeks after the pericardiolysis in Case 1. This rise persisted for several months; the venous pressure then returned to normal. In this patient there was relatively little improvement in the cardiac output following operation, though the output per beat was somewhat greater and the heart rate was slower. In Case 2 studies of the cardiac output could not be carried out after the operation because of the severe constrictive pleuritis which limited his breathing (Burwell and Ayer, 1941).

Several interesting spontaneous variations in the circulatory dynamics of these patients were encountered. First, a close relationship between the changes in the blood volume and the changes in the venous pressure was noted in Case 1. This is shown graphically in Fig. 2.

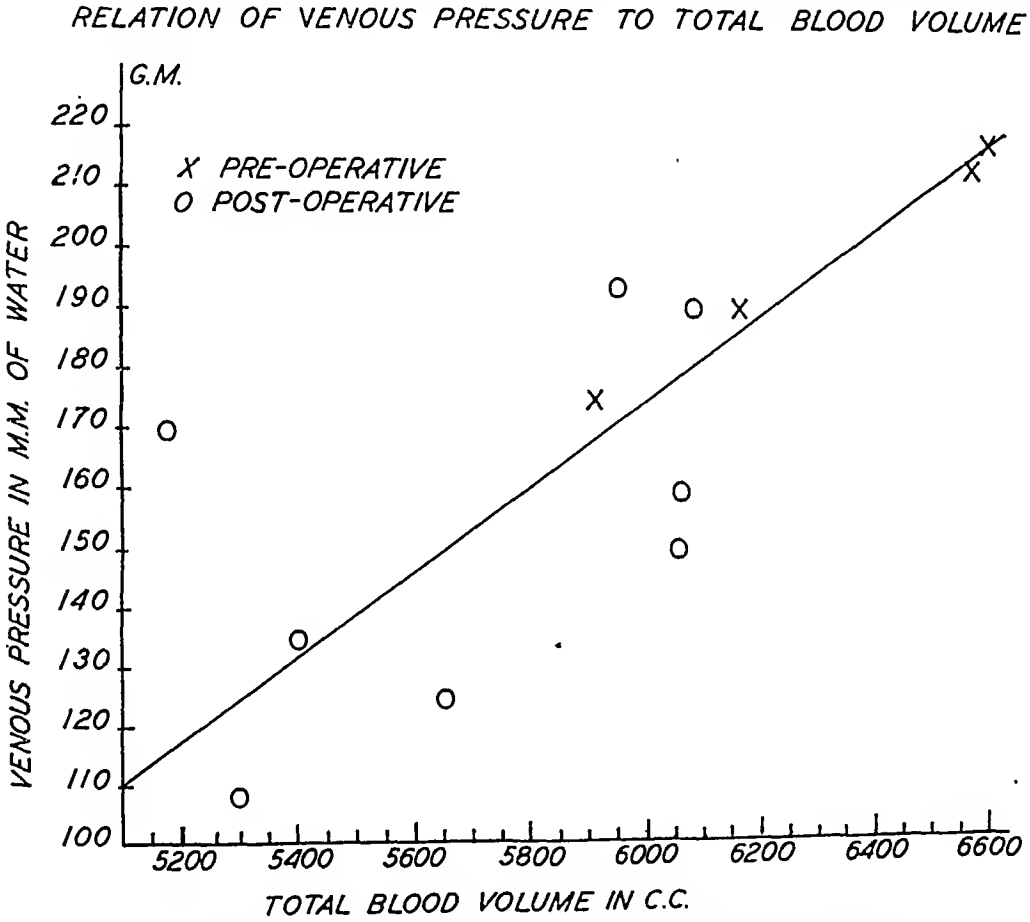

FIG. 2.—The relation of venous blood pressure to total blood volume in Case 1.

The relation may be expressed as: V.P. $= -239 + $ T.B.V. $(0{\cdot}069) \pm 18{\cdot}3$ mm. water. The correlation coefficient is $0{\cdot}83 \pm 0{\cdot}09$.

A similar relationship was apparent in Case 2, as seen in Table II. However, even with large spontaneous variations in venous pressure and blood volume no associated change was noted in the cardiac output per minute or per beat.

Second, there was considerable variation in the circulation time in both patients without corresponding change in the cardiac output or in the patients' general condition. In Case 1 a rough linear relationship was noted between the circulation time and the height of the venous pressure, as shown in Fig. 3. Case 2, who also had a high venous pressure and diminished cardiac output, usually had a prolonged circulation time but had several determinations within the normal range.

Third, when the heart rate increased there was a decrease in the output per beat in both patients. This was particularly evident in Case 2 who was completely digitalized at the start of his studies, and who showed a rise in heart rate when the digitalis was discontinued. The relationship between the heart rate and the output per beat is shown in Fig. 4. In his case,

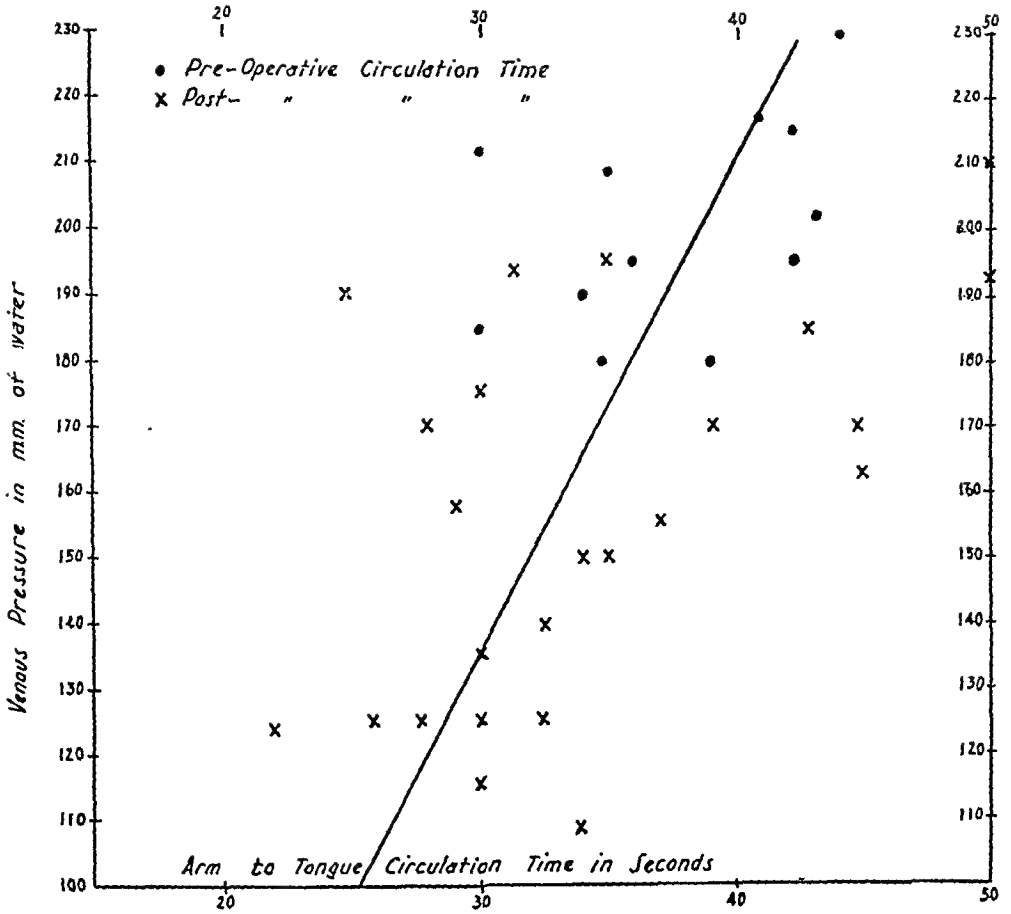

FIG. 3.—The relation of the circulation time and venous blood pressure in Case 1.

The relation could be expressed as: C.T.=11·86+V.P. (0·133)±5·8 sec. The correlation coefficient is 0·58±0·11.

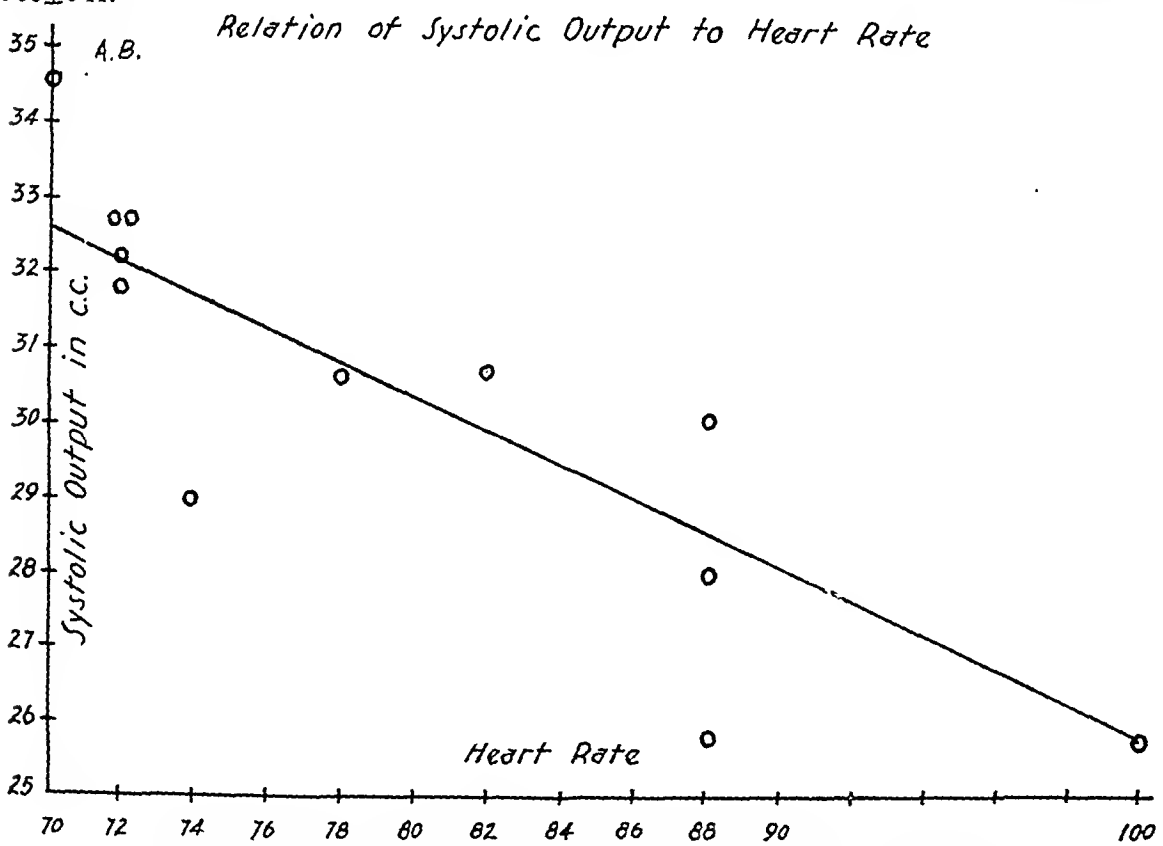

FIG. 4.—The relation of the heart rate and the output of the heart per beat in Case 2.

The relation may be expressed as: C.O./beat=49·1+heart rate (−0·235)±1·6. The correlation coefficient is 0·80±0·11.

even though there was a decrease in the output per beat, the output per minute showed a slight but progressive increase with the increased heart rate (Fig. 5). The same type of

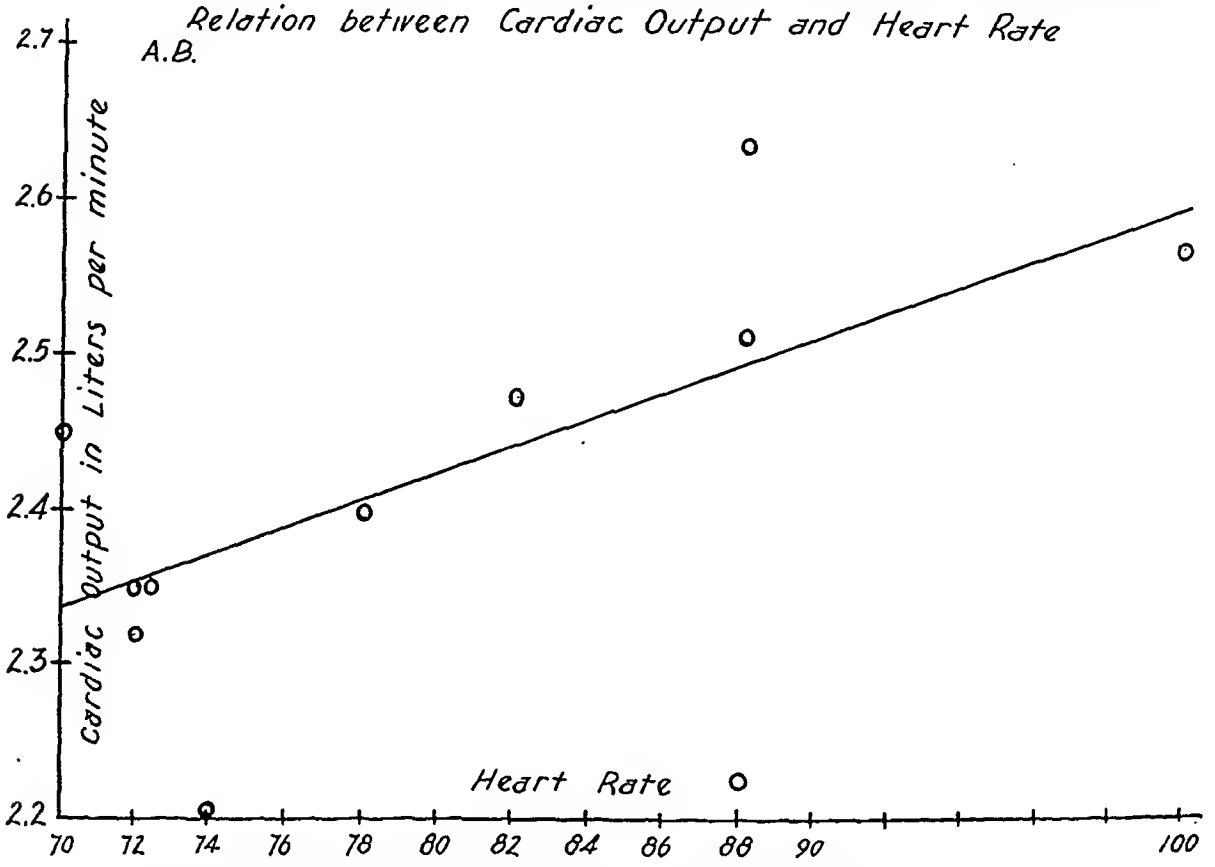

FIG. 5.—The relation of the heart rate and the output of the heart per minute in Case 2.

The relation may be expressed as: C.O./min.=1717·6+ heart rate (8·78)±112·5. The correlation coefficient is 0·57±0·2.

change was apparent in Case 1 but there was less variation in the heart rate and the changes were not so pronounced.

To amplify the observations made under standard conditions the following special studies have been carried out.

THE CHANGES IN THE CIRCULATION WITH CHANGES IN BLOOD VOLUME

It has been noted that there was a correlation between blood volume and venous pressure when spontaneous changes occurred. Such changes in blood volume and venous pressure were not reflected in alterations in heart rate or cardiac output. This observation led us to study the effect of rapidly induced changes in the blood volume.

After observing the effects of smaller amounts, 2900 c.c. of glucose and saline was administered by intravenous infusion in 45 minutes to Case 1. The results are recorded in Fig. 6. Although the venous pressure increased from 190 to 350 mm. of water there was no significant change in the cardiac output per minute or per beat. The heart rate increased only from 72 to 80. The circulation time was increased considerably at the middle of the infusion, and at the end of the infusion a 5 c.c. injection of sodium dehydrocholate failed to produce a reaction.

A similar infusion of 860 c.c. was administered to Case 2 in 15 minutes. There was a prompt increase in venous pressure from 185 to 325 mm. of water with the first portion of the infusion, followed by a gradual rise to 335 mm. with the last 150 c.c. In spite of a total rise of 150 mm. in the venous pressure there was no significant change in the cardiac output per minute. The output per beat fell from 34·6 to 29·7 c.c., while the heart rate increased from 70 to 76.

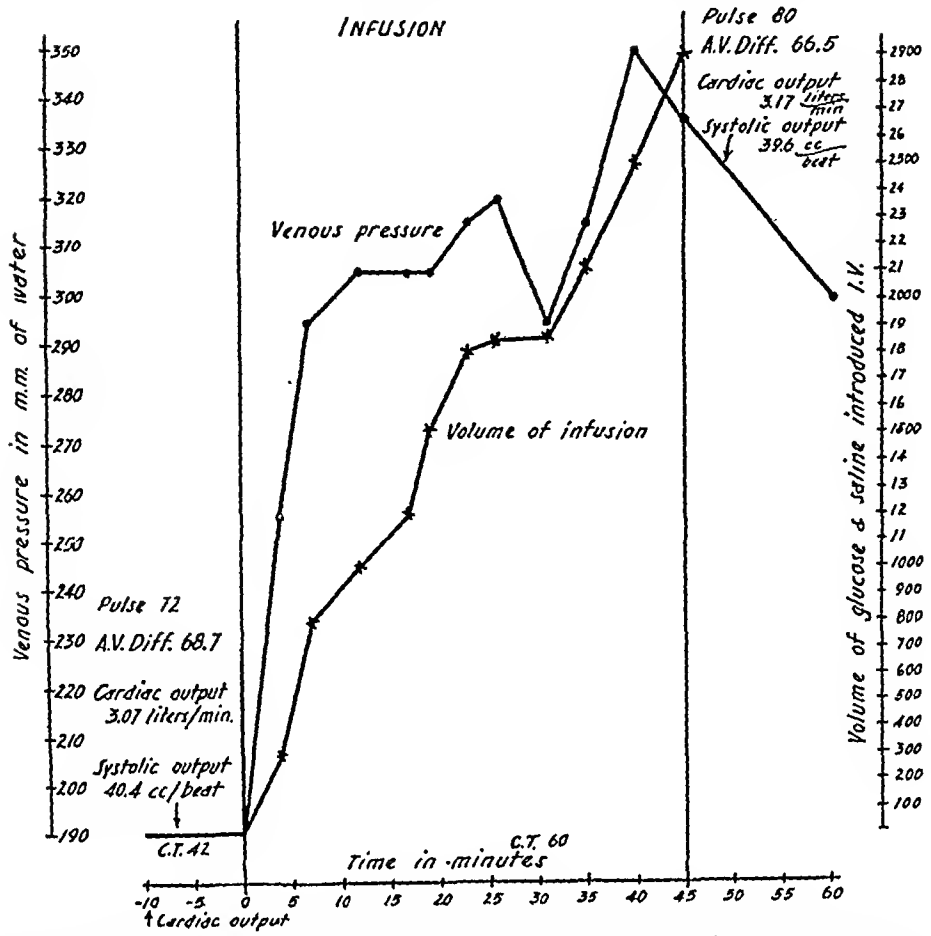

FIG. 6.—The effect of the intravenous infusion of fluid (5 per cent glucose in normal saline) on the venous pressure and on the output of the heart per minute and per beat, in Case 1.

Since a large increase in the venous pressure failed to alter the circulation significantly, the effect of induced decrease in venous pressure was then studied. After control measurements were made, blood (500 c.c.) was withdrawn over a twenty-minute period while the venous pressure, arterial pressure, and heart rate were observed. Immediately after the phlebotomy the cardiac output per minute and per beat were measured. The blood was then replaced and a third determination of the cardiac output made.

In Case 1 (see Fig. 7) there was a progressive fall in the venous pressure from 200 to 135 mm. of water during the removal of the first 300 c.c. of blood. The removal of an additional 200 c.c. lowered the venous pressure only 5 mm. further. The cardiac output per minute remained essentially unchanged. The heart rate changed from 72 to 76. The output per beat decreased only from 49·0 c.c. to 47·2 c.c. The replacement of the blood was associated with a slow but progressive rise in the venous pressure during the introduction of the first half of the infusion, and a more rapid rise toward the end until the venous pressure was 193 mm. of water. The patient, by this time, was somewhat disturbed by the long procedure. The oxygen consumption was elevated, the cardiac output was increased from 3·6 to 4·0 liters per minute, and the heart rate was 80. The circulation time remained essentially unchanged during the entire period.

A similar study of phlebotomy was made on Case 2 with generally similar results (Fig. 8). In this case, however, the venous pressure fell only 30 mm., from 215 to 185 mm. of water. As with Case 1 the venous pressure decreased during the removal of the first 300 c.c. of blood and it remained unchanged with the removal of an additional 200 c.c. The cardiac output per minute and per beat actually increased somewhat at the end of the phlebotomy which may represent a slight change from the basal state. With the re-infusion of the blood the venous pressure increased rapidly and progressively to 275 mm. The cardiac output, per minute and per beat, and the heart rate remained close to the initial determinations.

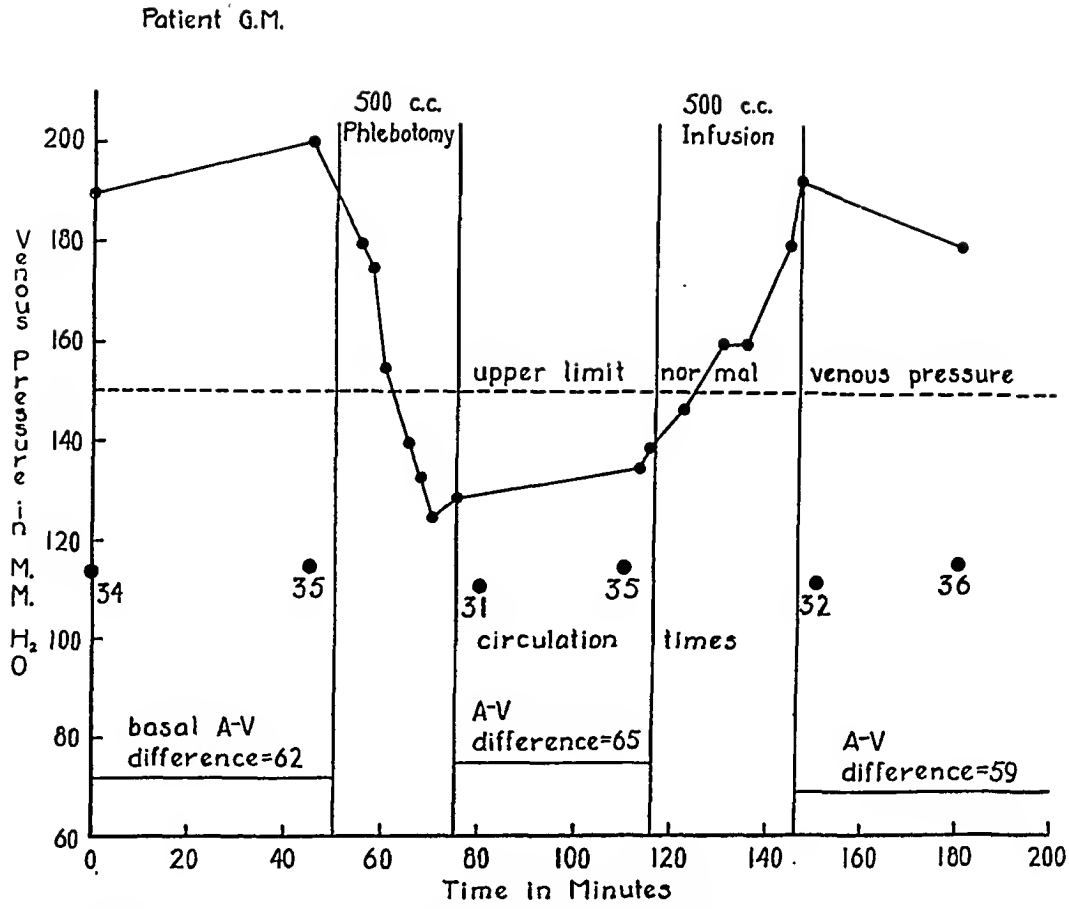

FIG. 7.—The effect of phlebotomy and re-infusion in Case 1 on the venous pressure, circulation time, and arterio-venous oxygen difference.

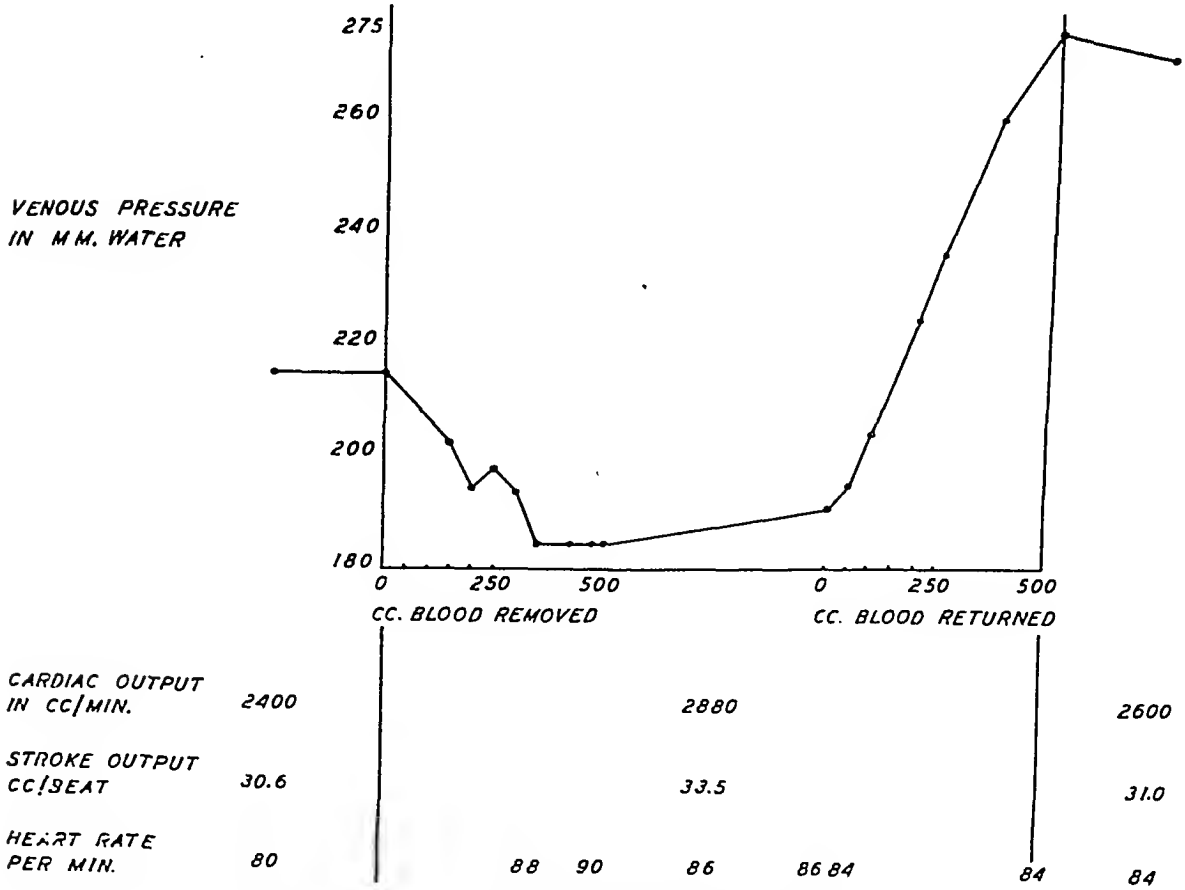

FIG. 8.—The effect of phlebotomy and re-infusion on the venous pressure, cardiac output per minute and per beat, and the heart rate in Case 2.

The Changes in the Circulation with Changes in Heart Rate

It was noted in the studies of spontaneous variation that when the heart rate was increased there was a decrease in the output of the heart per beat. In spite of this the cardiac output per minute was increased by such tachycardia, especially in Case 2. To test these observations further a transient tachycardia was produced by the intravenous injection of atropine sulphate so that comparable measurements of the circulation could be made immediately before and during the rapid heart action.

With Case 1 (Fig. 9), 3 mg. of atropine sulphate intravenously produced an increase in the

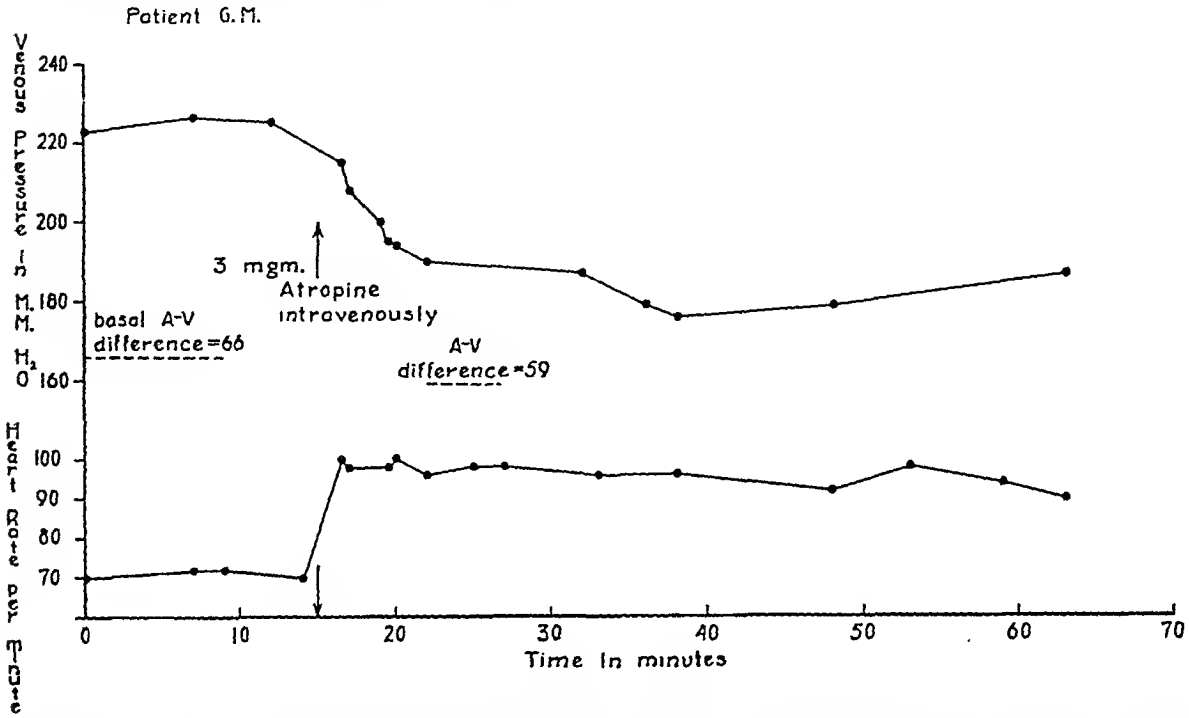

FIG. 9.—The effect of rapid rise in heart rate (induced by 3·0 mg. atropine sulphate intravenously) on the venous pressure and arterio-venous oxygen difference in Case 1.

heart rate from 70 to 98. With the onset of the tachycardia there was a fall in the venous pressure from 225 to 177 mm. of water, followed by a gradual return toward the control level as the tachycardia decreased. Although the output per beat decreased from 45 to 35 c.c., the output per minute was increased from 3·0 to 3·4 liters per minute. These observations were repeated a second time with essentially similar findings.

In Case 2, 4 mg. of atropine sulphate produced an increase in the heart rate from 72 to 94, and a fall in the venous pressure from 232 to 215 mm. of water. Although the output per beat decreased from 33 to 27 c.c., there was an increase in the output per minute from 2·35 to 2·7 liters. At the same time there was a slight increase in the vital capacity from 1800 to 2000 c.c., and a decrease in the circulation time from 36 to 26 seconds.

The effect of tachycardia that follows exercise was studied in Case 1. Immediately after a standard exercise the changes in the venous pressure and heart rate were observed. Fig. 10 is representative of the changes. There is considerable elevation of both venous pressure and heart rate at the end of exercise and both fall promptly with rest. The increased heart rate, however, continues for a considerable time, and is accompanied by a fall in venous pressure to a point below the initial resting level.

Discussion

It is accepted that the principal circulatory defect in constrictive pericarditis is limitation of diastolic filling of the ventricles. This results in a diminution of the output per beat. This is usually sufficiently severe to bring about a decrease in the cardiac output per minute even though a compensatory tachycardia may be present.

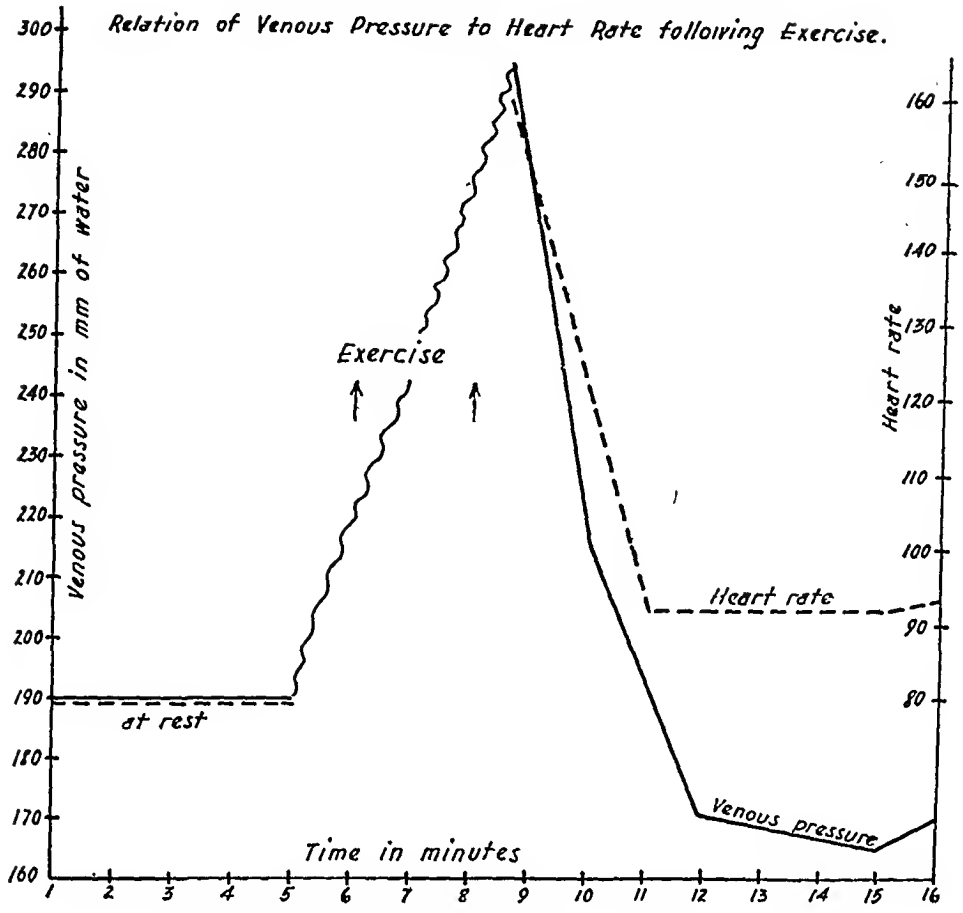

FIG. 10.—The effect of exercise on the venous pressure and heart rate of Case 1.

A question arises as to the effect of elevated venous pressure upon cardiac filling and cardiac output. When the heart is normal, a rise in venous pressure increases filling and output. What is the effect of such pressure change in the presence of pericardial obstruction? Where tamponade is due to pressure exerted by *fluid* in the pericardium (i.e. to a high intrapericardial pressure), an increase in venous pressure above some critical point may be expected to increase the flow of blood into the heart and so increase the cardiac output. This theoretical expectation is realized experimentally as is shown in a recent article by Cooper, Stead, and Warren (1944). Does the elevated venous pressure of constrictive pericarditis also assist in maintaining the circulation? It is apparent from our observations that large *spontaneous* variations of the venous pressure in these subjects have essentially no effect on ventricular filling as judged by alterations in the output per beat. *Induced* increases in the venous pressure of 160 and 150 mm. of water respectively, as a result of rapid infusion of glucose and saline, also failed to alter significantly the output per beat, the heart rate, or the output per minute. Rapidly induced decreases in the venous pressure of 60 and 30 mm. respectively also failed to affect the output per beat. That is, induced alterations in venous pressure over a total range of 220 and 180 mm. of water in these two patients did not influence the volume of the cardiac output. The conclusion that the high venous pressure of constrictive pericarditis is not effective compensation is in accord with expectation, since the obstruction to filling is not a high pressure (which may be overcome) but a non-distensible scar which puts a limit to dilatation of the ventricle during diastole.

It should be mentioned that while there was a progressive fall in the venous pressure of both patients during the first 300 c.c. of the phlebotomy, the further removal of 200 c.c. of blood failed to induce corresponding changes in the venous pressure. This sudden change in rate of fall in venous pressure during phlebotomy implies the operation of some compensatory mechanism. It may be that venous constriction occurs at that level and tends to prevent a further fall in the pressure.

The wide fluctuation in the venous pressure noted in following the course of those patients

appears to be related to changes in the volume of the blood and not directly related to changes in cardiac output. The elevation of the blood volume in these cases is similar in degree to that found in congestive heart failure and is probably due to similar mechanisms, one of which may be the abnormal retention of sodium. With such a retention of sodium either in normals (Lyons, Jacobson, and Avery, 1944) or in cardiacs, there is a resultant elevation of the blood volume and an increase in the venous pressure. The elevation of the venous pressure in Case 2 following the ingestion of large amounts of salt (Table II), and the fall in the venous pressure after ammonium chloride and mercupurin, suggest that the sodium balance may be an important factor in the control of venous pressure in such patients.

In most cases of constrictive pericarditis important manifestations are œdema, ascites, and pleural effusion. Presumably these result chiefly from the elevated venous pressure. These may be successfully influenced in the milder cases by a low sodium intake and occasional diuretics. In more severe cases the venous pressure cannot be lowered sufficiently to prevent the development of transudates, even with extensive diuresis.

The tachycardia noted in these subjects may well represent a mechanism tending to compensate for the diminished cardiac output per beat imposed by the limitation of diastolic filling. The increase in the cardiac output per minute and the decrease in venous pressure after induced tachycardia suggest that a rapid heart rate may be beneficial under these circumstances. Conversely a bradycardia may be injurious. Burwell and Strayhorn (1932) observed a patient in whom a decrease in the heart rate of 16 beats per minute, the result of digitalization, was associated with a fall in the cardiac output of 580 c.c. per minute. Similarly, in Case 2, the heart rate and cardiac output increased after digitalization was stopped. It is probable that digitalis has only an occasional place in the medical management of these patients with a regular rhythm, not only because of its effect on the heart rate, but also because it cannot alter the cardiac output through improvement in muscle tone since the heart is constricted rather than dilated. Exceptions to this rule may be found in patients with auricular fibrillation and many inefficient ventricular contractions, and in patients who have myocardial dilatation following relief of the constrictive pericarditis.

Increase in the heart rate is the only way in which these patients can increase the cardiac output (e.g. during exercise), since the associated elevation of the venous pressure fails to increase filling. The effect of tachycardia following exercise is similar to the effect of tachycardia produced by atropine in its ability to lower the venous pressure below the control level. This is not to say that an unlimited degree of tachycardia is desirable for these patients. There is probably an optimum rate in each individual, which is neither too high nor too low. Experience with patients having constrictive pericarditis *and* auricular fibrillation indicates that this optimum rate is considerably slower than the usual ventricular rate in uncontrolled auricular fibrillation.

Summary

Observations of the alterations in venous pressure, blood volume, heart rate, cardiac output per beat and per minute, circulation time, and vital capacity have been recorded for one patient with constrictive pericarditis who was studied for three years prior to pericardiolysis and for six years after the operation. Similar observations have been made on another patient with a more profound disability for a shorter time.

The spontaneous fluctuations in the venous pressure in these patients were not related to alterations in the cardiac output per minute or per beat, but appeared to be closely correlated with variations in the blood volume. It appears likely, therefore, that such fluctuations in venous pressure in these patients reflect changes in the water content of the body.

Increases in venous pressure of 160 and 130 mm. of water above the control level was produced in the two patients by the intravenous infusion of glucose and saline. These increases failed to alter the heart rate or the cardiac output per beat and per minute.

Decreases in the venous pressure of 60 to 30 mm. of water as a result of a 500 c.c. phlebotomy also failed to alter the cardiac output per minute and per beat.

Spontaneous increases in the heart rate were associated with decreases in the output per

beat, and with a slight net increase in the cardiac output per minute. Tachycardia produced by the intravenous injection of atropine sulphate was accompanied by an increase in the cardiac output per minute and a fall in the venous pressure. Tachycardia following exercise produced a similar decrease in the venous pressure below the resting level.

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PARAVERTEBRAL BLOCK AND THE ELECTROCARDIOGRAM IN ANGINA PECTORIS

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Received October 21, 1945

Various surgical procedures in the region of the cervico-thoracic sympathetic system have been proposed for the treatment of angina pectoris. The paravertebral block of the upper thoracic sympathetic ganglia proved to be the most successful and the least dangerous. It was first introduced by Mandl (1925) who, using injections of novocain, reported that he had achieved relief of pain for many weeks. Swetlow (1926) recommended the use of alcohol and thought by this modification to prolong the effect of the paravertebral block. The sensory nerves of the heart and coronary vessels pass through the middle and inferior cardiac nerves to the middle and inferior cervical ganglia. Since there are no white rami communicantes between the cervical sympathetic chain and the spinal cord these sensory fibres must descend to the upper thoracic ganglia, from where they finally reach the spinal ganglia (Ranson and Billingsley, 1918, and Stohr, 1928). Besides the cervical cardiac nerves, there exist thoracic cardiac nerves which also serve as sensory pathways (Brauecker, 1927; Jonescu, 1927; and White *et al.*, 1933): these nerves pass directly through the posterior mediastinum to the upper four or five thoracic sympathetic ganglia. Thus, all the sensory pathways from the heart converge, uniting in the upper four or five thoracic ganglia. These anatomical facts explain the good results obtained by the paravertebral block of the upper thoracic ganglia (Marvin, 1935; Ochsner and DeBakey, 1937; and Levy and Moore, 1941).

Objections against any surgical intervention in the sympathetic nervous system as a method of treatment in angina pectoris have been raised by Danielopolu *et al.* (1931). They expressed the view that the sympathetics serve as vasodilators of the coronary vessels. Therefore, interruption of the sympathetic innervation may decrease the coronary flow and be even dangerous for a patient suffering from angina pectoris. Experimental studies on animals after ligation of the main coronary branches when the stellate ganglia or the thoracic ganglia have been removed do not, however, support this contention (Averbuck and Rachmilewitz, 1931: and White *et al.*, 1933). On the contrary, it has been reported that under these conditions there is a decrease in the mortality rate of the animals after ligation of the main branches of the coronary arteries (Leriche *et al.*, 1931).

The effect of the interruption of the sympathetic nerves on the coronary circulation in man is of special importance. Since in man coronary flow cannot be measured directly the use of the electrocardiograph affords the only method of revealing changes in the coronary circulation. The paper of Levy and Moore, who in 1941 reported their results in the treatment of cardiac pain by the paravertebral block contains also electrocardiographic observations. In 16 out of 45 patients cardiograms were taken and in 14 improvement was found. They assumed that the modification of the cardiogram indicated altering conditions in the coronary circulation.

The present investigation was carried out to study the effect of the paravertebral block on the electrocardiogram in cases of angina pectoris. A series of cardiograms was made in 12 patients treated by this method before and after the block. In 7 of them records were taken immediately before and twenty-four hours after the first injection to ascertain the

immediate effect of the block. All patients were suffering from severe anginal pain and were under medical observation for some time before they were subjected to this treatment. The treatment consisted of 4–7 paravertebral injections, the interval between each of them being three to six days. For the first injection novocain only was used while the following injections were performed with novocain and alcohol.* Eleven patients showed cardiographic changes before the block. Three of these did not show any improvement of the cardiogram after the block. In the first the cardiogram showed signs of bundle branch block, in the second signs of a recent myocardial infarction of the posterior wall, and in the third four negative T waves. In eight cases the cardiogram showed an improvement after the paravertebral block. The cardiographic changes in these cases were mainly concerned with the final deflection. Abnormalities of the T wave in at least two leads were present in all of them. The T waves were negative, iso-electric, diphasic, or flattened. In some cases there was also a depression of the S–T segment. After the paravertebral block the T waves became positive or more elevated and the S–T depression disappeared. In four cases this positive effect was observed already twenty-four hours after the block, but the maximum improvement of the electrocardiogram was generally obtained at the end of the treatment.

Table I gives an account of the cardiographic changes that took place as the result of the paravertebral block. The degree of elevation of the T waves following this treatment was designated as + corresponding to an elevation of 0·5 mm. ± 0·25 mm.; as ++ corresponding to an elevation of 1·0 mm. ± 0·25 mm.; and as +++ corresponding to an elevation of 1·5 mm. ± 0·25 mm.

TABLE I

Case No.	Sex and Age	Electrocardiogram	
		Before treatment	At the end of treatment
1	M. 46	S–T I and IV depressed, T I, T IV inverted	S–T I and IV iso-electric, T I upright ++, T IV upright +++
2	F. 48	T I, T IV iso-electric	T I upright +++
3	M. 51	T I iso-electric, T IV flat, P–R 0·25, QRS 0·13 sec.	T I upright ++, T IV upright ++
4	M. 57	S–T I depressed, T I inverted, T II, T IV flat	S–T I iso-electric, T I upright ++, T II upright ++, T IV upright +++
5	M. 51	S–T II depressed, T I inverted, T II, T III iso-electric	S–T II iso-electric, T I upright +, T II upright +
6	M. 44	T I flat, T IV inverted	T I upright, +, T IV iso-electric
7	M. 52	S–T I and II depressed, T I, T IV diphasic, T II flat	S–T I and II iso-electric, T I upright ++, T II upright +++,
8	M. 48	S–T I and II depressed, T I inverted, T II iso-electric	S–T I and II iso-electric, T I upright +, T II upright +

A few typical case histories are given.

Case 3. J. A., aged 51, was admitted to the hospital on February 20, 1945. He was suffering for two years from attacks of pain in the præcordium with radiation to the left shoulder and arm. In the last seven months these attacks appeared very frequently, after the slightest effort and then even at rest, and therefore the patient was confined to bed for most of the time.

The clinical and X-ray examinations of the heart did not reveal any pathological findings apart from slight enlargement of the left ventricle. The blood pressure was 140/115. After ten days of observation, during which period the patient continued to suffer from anginal pain, the first paravertebral injection with novocain was done. Immediately after this procedure the pain subsided but appeared again a few days later. During one month five paravertebral injections with novocain and alcohol were performed. At the end of this period the pain disappeared.

A cardiogram done on the day before the paravertebral block showed left axis deviation, a prolonged P–R interval (0·27 sec.) and a slightly widened QRS in leads II and III. The T waves in the first lead were absent and in the fourth lead flat (Fig. 1A). Twenty-four hours after the first paravertebral injection the T wave in the first lead became positive (Fig. 1B). At the end of the treatment

* A detailed description of the technique is given in F. Mandl, *Paravertebral and Splanchnic Block*, Grune and Stratton, New York, 1945.

the T waves in the first and fourth lead became normal while no change took place in the prolonged P–R interval (Fig. 1c).

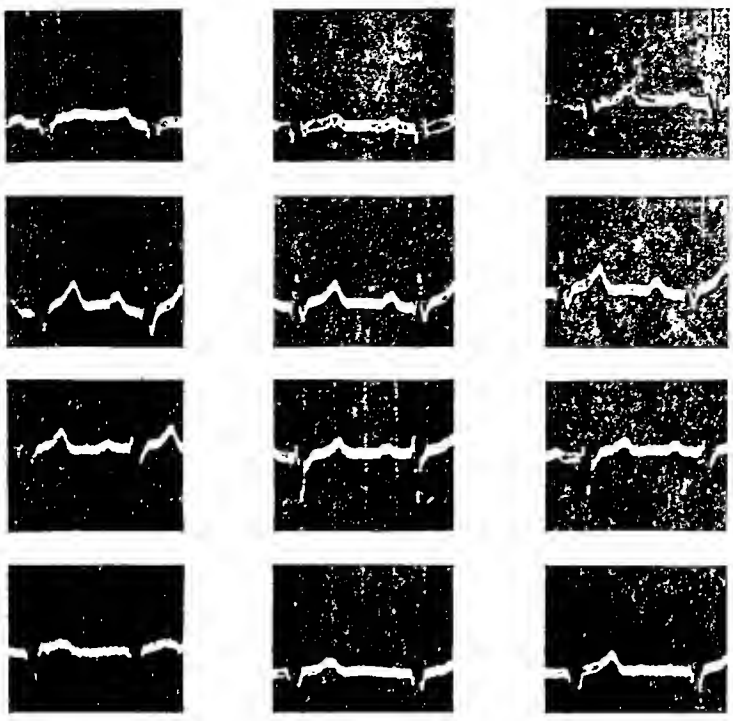


FIG. 1.—Case 3. (A) Iso-electric wave in lead I and flat T wave in lead IV. (B) Twenty-four hours after the paravertebral block; T I positive. (C) At the end of the treatment; elevation of T I and T IV. No change in the P–R interval and in QRS after the treatment.

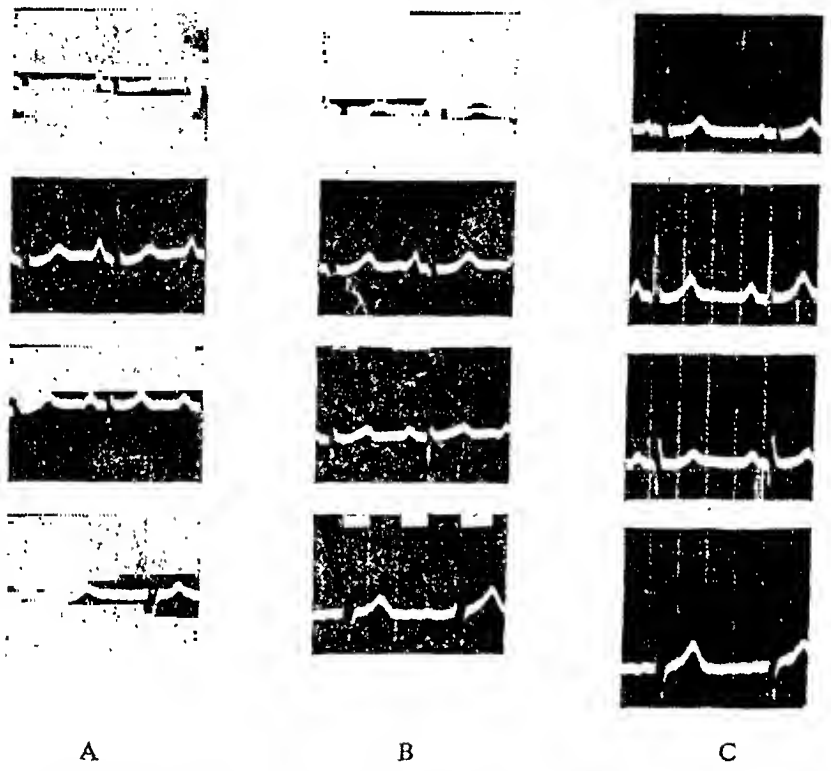
Case 4. P. R., aged 57, was admitted on January 23, 1944. Two and a half months before admission the patient had had an attack of severe pain in the præcordium. Since then he was suffering from continuous pressure in this region. Every effort or emotion increased the pain; even the shortest talk and the intake of food could precipitate an attack. His blood pressure was 140/100. The X-ray of the heart was normal. The patient was observed for one week during which period aminophyllin and sedatives were given. In spite of complete rest and the medical treatment he continued to suffer from frequent attacks of angina pectoris. On February 1, the first paravertebral injection of the upper two thoracic ganglia was done. This resulted in a marked relief of pain. During a period of three weeks seven injections with novocain and alcohol in the upper four thoracic ganglia were performed. At the end of this period the patient was practically painless.

Two cardiograms were made before the paravertebral block was performed and both of them showed the same pathological changes. The T waves in the first lead were slightly negative and flat in the other leads (Fig. 2A). After the first paravertebral injection the T waves in the first lead became low, upright and higher in the other leads (Fig. 2B). At the end of the treatment the cardiogram was practically normal (Fig. 2C).

Case 6. J. F., aged 44, was admitted on September 3, 1944. Six months before admission, after an effort the patient experienced an acute sharp pain in the chest which continued for a few hours. This attack was accompanied by severe dyspnœa. Since then the patient was suffering from repeated attacks of anginal pain which appeared after walking and the slightest effort. He was sent to our department in July, 1944, but because of an intercurrent febrile disease a paravertebral block could not be performed at this time. During the course of the disease numerous cardiograms were taken and there was a suspicion that the first attack of pain was caused by a myocardial infarction (anterior wall). In the last month the cardiographic tracings showed identical changes. On clinical and X-ray examinations a slight dilatation of the left heart was found. The blood pressure was 140/90. The heart sounds were normal. The laboratory examinations did not show any pathological findings. On September 5, a paravertebral block with novocain was done. The first and second thoracic segments were injected. Shortly after the injection anæsthesia and paresis developed in the left arm and hand. Because of this complication the paravertebral block was not continued. The pain in

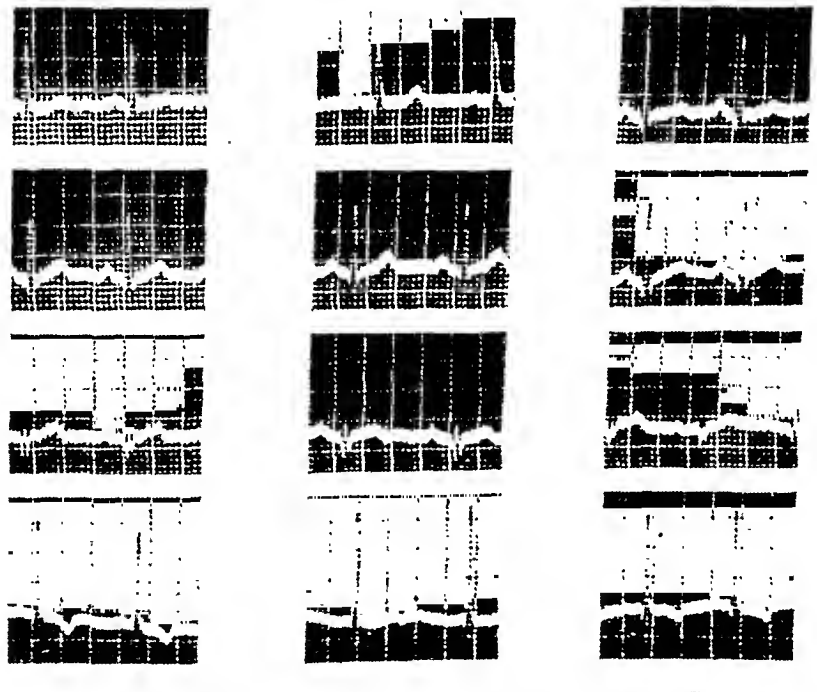
the chest disappeared completely after the injection, and while staying in the hospital for another month the patient did not feel any pain.

Immediately before the paravertebral block was performed a cardiogram was taken which showed left axis deviation, flat T waves in lead I, and inverted T waves in lead CF 4 (Fig. 3A). Twenty-four hours after the paravertebral block the cardiogram showed a change. The T waves became higher,



A B C

FIG. 2.—Case 4. (A) Negative T wave in lead I, flat T wave in lead II and IV, S-T II depressed. (B) Twenty-four hours after paravertebral block; T I positive, T II and T IV more elevated, S-T II iso-electric. (C) At the end of the treatment, the cardiogram shows further improvement and is practically normal.



A B C

FIG. 3.—Case 6. (A) T wave in lead I flat and in CF 4 negative. (B) After novocain block; T I more elevated, T IV iso-electric. (C) Twenty-four hours later, the cardiogram shows the same changes as before treatment. The improvement was only temporary.

upright in the first lead and iso-electric in the fourth lead (Fig. 3B). One day later the cardiogram showed the same pathological changes as before the paravertebral injection (Fig. 3C). The improvement was only temporary, and two days after the paravertebral injection the cardiogram showed the same changes as before the treatment.

COMMENT

The electrocardiographic changes found in our cases before treatment were concerned especially with the T waves, alterations that are generally believed to be caused by anoxæmia of the myocardium due to a diminished coronary flow. The most frequent causes of a diminished coronary flow are arteriosclerosis and spasm of the coronary vessels. Anoxæmia is according to the present concept the chief cause of cardiac pain (Keefer and Resnik, 1918; Sutton and Lueth, 1930; Rothschild and Kissin, 1933; and Levy *et al.*, 1938). While the relief of pain achieved by the paravertebral block can be explained by the interruption of the sensory pathways, the improvement of the cardiogram is most probably produced by an increased coronary blood flow and a greater oxygen supply to the heart muscle. The mechanism by which the improvement of the coronary circulation is achieved deserves special comment. It is agreed that the vasoconstriction of the peripheral vessels is mediated by the sympathetic nerves. But there is a discrepancy of opinion regarding the innervation of the coronary arteries. Leriche *et al.* (1931) assumed that the innervation of the coronary vessels follows the general law of vasomotor innervation and thought to have proved it by experiments in dogs: they ligated the descending branch of the left coronary artery at various levels and found that after ligation at higher levels the animals died from ventricular fibrillation, while after removal of both stellate ganglia the animals survived. Katz and Jochim (1939) found that cutting the sympathetic supply to the heart usually produced a coronary vasodilatation, sometimes, however, a vasoconstriction was noted; they concluded that the stellate ganglia send to the heart adrenergic coronary dilator and adrenergic coronary constrictor fibres. Evidence has also been accumulated indicating that the innervation of the coronary arteries is different from that of the systemic vessels. Anrep and Segall (1926) first showed that the vasoconstrictor fibres are carried chiefly in the vagus while the sympathetic nerves contain the vasodilator fibres. A series of investigations by improved methods confirmed these findings (Green *et al.*, 1942; Essex *et al.*, 1943). Recently also Gregg and Shipley (1944) showed that stimulation of the stellate ganglia and their cardiac branches causes an increase in the coronary blood flow.

The clinical experience with paravertebral block as a method of relieving pain in angina pectoris and our observations indicate that the blocking of the upper thoracic sympathetic ganglia may cause an improvement of the coronary circulation. The change of the cardiogram following this procedure furnishes objective evidence for the beneficial effect on the coronary blood flow. The improved circulation may be a direct sequel of the blocking of the sympathetic or the relief of pain may cause an abolition of reflex spasm in anatomically unaffected vessels and thus a dilatation of coronary vessels; this last possibility was assumed by Levy and Moore (1941). In our series of cases there was not always a parallelism between the improvement of the cardiogram and the persistence and severity of cardiac pain. In one of our patients (Case 6) a block with novocain of the upper two thoracic ganglia only was performed: in this case there was an improvement of the cardiogram for twenty-four hours: but afterwards it showed the same changes as before treatment although the patient was relieved from his cardiac pain for several months. In other cases the cardiogram remained improved many months after the paravertebral block although the patients suffered again from attacks of angina pectoria.

In the three cases in which no improvement of the cardiogram after the treatment was observed, the cardiogram showed marked pathological changes (bundle branch block, myocardial infarction, and inverted T waves in four leads). It may be assumed that in these cases the changes in the cardiogram were caused by severe anatomical alterations in the coronary vessels and therefore no improvement could take place.

SUMMARY

In twelve patients suffering from frequent attacks of angina pectoris the electrocardiogram was studied before and shortly after the paravertebral sympathetic block. Out of eleven cases with cardiographic abnormalities before the block, eight showed an improvement of the cardiogram. The T waves which before the block were flat, diphasic, iso-electric, or negative showed a tendency to return to normal. The improvement of the cardiogram did not always coincide with the relief of pain.

We take the opportunity of thanking Prof. F. Mandl and Dr. H. Melwidski, who performed the paravertebral injections.

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ELECTROCARDIOGRAPHIC ABNORMALITIES IN SEVERE MALNUTRITION

BY

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Approved for publication by the Office of the Chief Surgeon, European Theatre of Operations, U.S. Army

Received October 4, 1945

Just before and after V-E day a major medical problem in the European Theatre of Operations was the care of the great number of liberated Allied prisoners of war. Many of these were suffering from profound and prolonged malnutrition and the gravity of their physical condition, coupled with the great numbers involved, taxed the resources of the medical personnel caring for them. Numerous studies of various aspects of the physiological derangements of these soldiers have been made. This report is concerned with electrocardiographic findings in a small series of severely malnourished patients.

During the night of April 24, 1945, a trainload of 300 fresh casualties reached a U.S. Army General Hospital in England. Among these were a few severely malnourished liberated American prisoners of war. One of these, S/Sgt. A. A., appeared to be in such a critical state that it seemed unlikely that he would survive many hours. He was semi-stuporous, so weak he could hardly lift a hand, emaciated to a degree which has become all too familiar in photographs of the " Horror Camps," and suffering from intense diarrhœa. In spite of this he showed no œdema, his blood pressure was normal, and there was no clinical evidence of any vitamin deficiency. On admission it was noted that his pulse rate was 40 at the wrist and about 60 at the apex. This led to the taking of a cardiogram the following morning. Because of the striking findings in this record (Fig. 1), serial records were made on this patient and on 13 other liberated prisoners who were the most severely malnourished.

Some days after admission the first patient was interviewed by a reporter from the *Stars and Stripes*. Excerpts from this interview are reproduced here as they depict in graphic terms the conditions which produced the physical state of all of these men.

U.S. GENERAL HOSPITAL. The day the Nazis took S/Sgt. A.A., 106th Infantry Division squad-leader, prisoner, he weighed 210 pounds. Five months later, when liberated, he weighed 116 pounds. Considering the hell he's been through, he is coming along fine. But thanks to Himmler's S.S. he won't be walking around for some time. Here's what he told me :

" I was captured at St. Vith during the Rundstedt breakthrough. The Nazis searched me, and put me in a box-car with 42 other Yanks. They locked us in, sending us on our way to Germany.

" For five days and nights we didn't have any food or water. Luckily, some of our fellows still had a little water in their canteens—just enough to wet 43 parched mouths. We didn't dare drink the stuff; it was too precious. Added to this, the convoy we were in was being bombed and strafed continually by the Allies.

" We were sent to Camp 4b, 50 miles south of Berlin, and then to Camp 8a, near Gorlitz. Camp 4b was better to us. At least they didn't abuse us so much. Finally, they started us on the march because the Russians were advancing We got very little to eat on the march, but we usually got plenty of water. If there weren't any rivers or streams around the Russians or " Froggies " always brought it to us in buckets. If our guards caught them, they used to beat them, but most of them were smart. They used to leave the buckets on the side of the road and hide until we went by.

" I don't remember just how far we'd marched when the Yanks caught up with us. What I do remember, I was lying on top of a straw and manure pile when they found me, and I was pretty well gone."

Clinical abstracts on this and three other patients showing the most striking electrocardiographic changes follow.

Case Notes

Case 1. Staff Sgt. A. A., 29 years old, was captured on December 19, 1944, and released on April 13, 1945, eleven days before he entered the hospital. In addition to the account of his experiences quoted above, the following information is relevant. While a prisoner he had lived on the regular prison diet, which consisted of a sixth to an eighth of a loaf of bread, soup which occasionally contained a little meat, and a few potatoes daily. In addition, while marching, he received some jam and one-ninth of a tin of meat weekly. In spite of his steady loss of weight he got along pretty well until February, since which time he was almost constantly on the march, averaging about 20 kilometres a day. Three days before he was liberated he developed diarrhœa and abdominal cramps, and very rapidly went down hill from then on. He lost weight estimated at 100 lb. while a prisoner.

His past history was irrelevant; he was always a very healthy and vigorous person. Physical examination showed extreme emaciation, weakness, and semi-stupor. There was no œdema nor any evidence of vitamin deficiency. His tongue was normal and his skin though dirty showed no evidence of hyperkeratosis. The lungs were clear, the heart sounds were faint, and there was an apical systolic murmur. His blood pressure was 110 mm. systolic and 60 mm. diastolic.

Laboratory findings are shown in Table I. In addition the plasma albumin was 3·6 and globulin 2·0 per 100 c.c. on May 5. Urine analysis was normal except for a one-plus albumin on entry. A radiogram of the chest showed the lung fields to be clear and the heart unusually small, and one of the hands and forearms showed no evidence of decalcification. Cardiograms are shown in Fig. 1, 2, and 3.

TABLE I

Laboratory and Cardiographic Findings on Cases 1–4

Case No.	Date	Hæmoglobin Grams /100 c.c.	Plasma proteins Grams /100 c.c.	Serum Ca. mg. /100 c.c.	Serum P mg. /100 c.c.	Electrocardiograms			
						P–R interval sec.	QRS interval sec.	Q–T interval * sec.	T waves
1	April 25	13·3	6·2			0·19–0·20	0·12	0·70 (+0·28)	T II TIII up with low origin †
	April 30			10·2	1·5	0·19	0·11	0·60 (+0·18)	T II TIII diphasic with low origin T IV diphasic
	May 3					0·19	0·09	0·50 (+0·14)	T II T III diphasic
	May 5	10·9	5·6	10·2	3·2				
	May 8					0·19	0·08	0·38	T II up T III inverted
	May 16					0·18	0·07	0·33	All T waves upright
2	April 25	13·5	6·7			0·21	0·09	0·52 (+0·14)	T I T II T IV bifid
	April 28					0·18	0·08	0·54 (+0·16)	T IV bifid
	April 30			9·5	1·6	0·22	0·08	?0·50	T IV bifid
	May 5		5·1	8·7	3·3				
	May 8					0·18	0·08	0·37	All T waves upright
3	April 25	16·8	8·0						
	April 29					0·12	0·08	?0·48 (+0·14)	T I isoelectric T II T III inverted
	May 3	14·9		9·0	1·5	0·12	0·08	0·48 (+0·14)	T II T III low origin
	May 7					0·12	0·08	0·34 (+0·02)	Slight depression S–T II and T III
	May 16					0·12	0·07	0·32	All T waves upright
4	April 26	11·1	5·5			0·14	0·07	0·38 (+0·04)	Bifid T IV
	May 5			9·1	4·0				
	May 10					0·14	0·06	0·33	Normal T waves

* Figures in parentheses refer to increase in Q–T above the maximum allowable by the standards of Ashman (1942). Measurements were made from start of QRS to return to the iso-electric level after the T waves and may include U waves.

† Ventricular premature beats every third beat.

His diarrhœa and cramps continued for about a week. For the first few days he was unable to take nourishment by mouth, except in extremely small quantities. He was given 2 units of plasma and 1000 c.c. of 5 per cent glucose in normal saline solution daily for three days. His temperature, which was sub-normal on entry, rose to 103 degrees by May 2 and remained up for several days, although at this time he had very greatly improved. He gained an estimated 20 lb. during this first week, this being largely due to improvement in hydration. On May 4 he was allowed to sit in a chair and by May 16 to walk short distances. He was given a 500 c.c. blood transfusion on May 8.

Case 2. Pte. B. P., 23 years old, was captured on December 21, 1944, and released on April 13, 1945. His history was very similar to that of the first patient. The diet he was given was exactly the same and he suffered from severe diarrhœa for about two weeks before his release. Physical

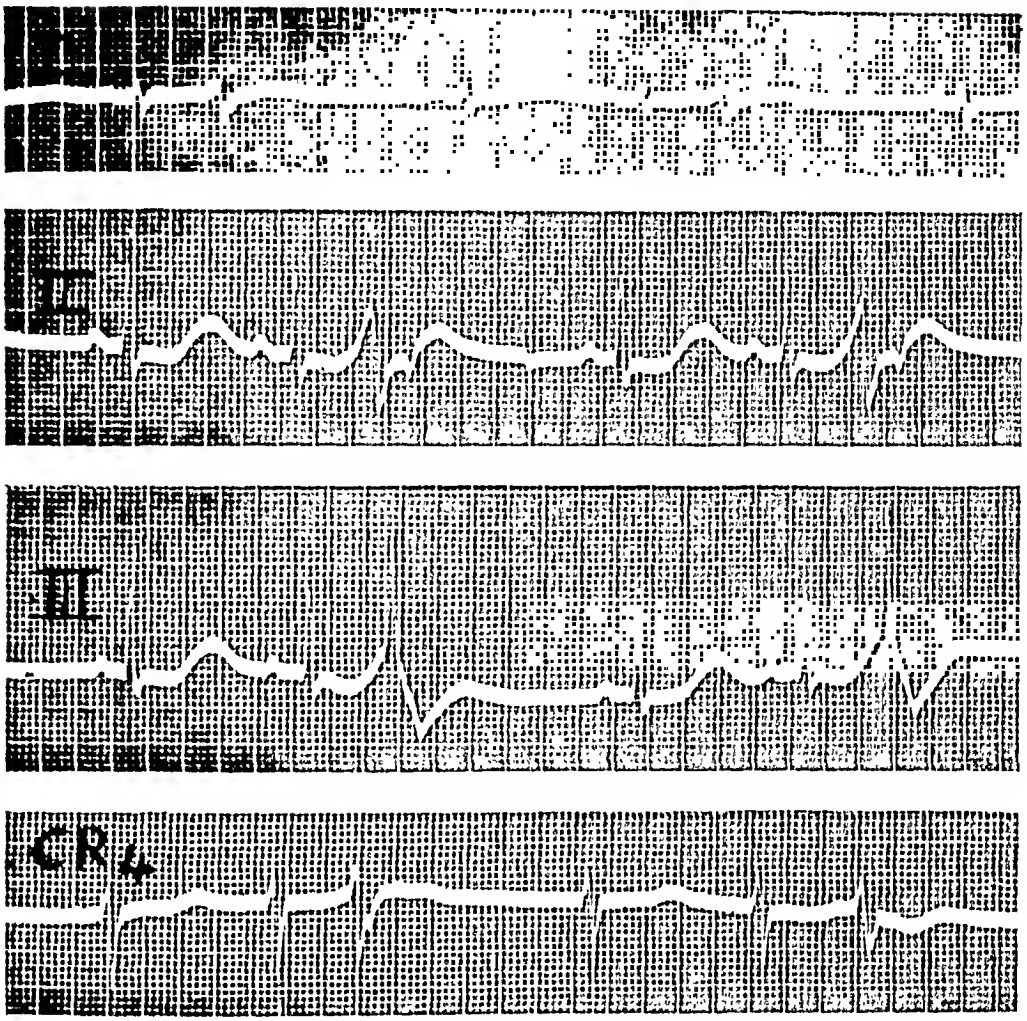

FIG. 1.—Electrocardiogram of Case 1. 25/4/45.

examination showed extreme malnutrition with an estimated loss of 64 lb. in weight during his confinement. He, however, was admitted as an ambulatory patient and was perfectly clear mentally. Physical examination on entry showed no œdema nor signs of vitamin deficiency. The heart was normal on examination, with normal sounds and no murmurs. Blood pressure was 110/70.

Laboratory findings are shown in Table I. In addition the urine analysis was normal, except for a one-plus albumin on entry. The plasma albumin was 4·1 on April 25 and 3·5 on May 5, and the globulin 2·6 and 2·1 per 100 c.c. on the same dates. A radiogram of his heart showed it to be rather small, and one of his hands and forearms showed no evidence of decalcification. Fig. 4 shows the cardiograms.

By April 30 he was much better and his diarrhœa had ceased. He was eating well, as he had since the beginning of his stay in hospital, and never required any intravenous fluid administration. On April 30 he developed some œdema of the ankles which persisted for about ten days. On this date also he noted that he had cramps of the hands and legs, and when he tried to write, his right hand went into spasm. Examination revealed carpo-pedal spasm after exercising his hands or feet and a positive Trousseau sign but a negative Chvostek sign. There were some fibrillary twitchings in the forearms. These signs persisted for about four days. At this time his blood calcium was normal, he was well hydrated and there was no clinical evidence of alkalosis, but the carbon dioxide combining power of the blood could not be done. His improvement continued thereafter in an uninterrupted manner, except that on May 16 he developed mild jaundice which was interpreted as being due to infectious hepatitis. This persisted for about a week only.

Case 3. Cpl. R. D., 25 years old, was captured on December 19, 1944, and released April 16, 1945. His history was much like the others except that he had not been forced to undergo any marching during the months before his release. He had had diarrhœa for about a week before his release. Upon entry he appeared to be in fair physical condition but had lost 30 lb. in weight. The blood

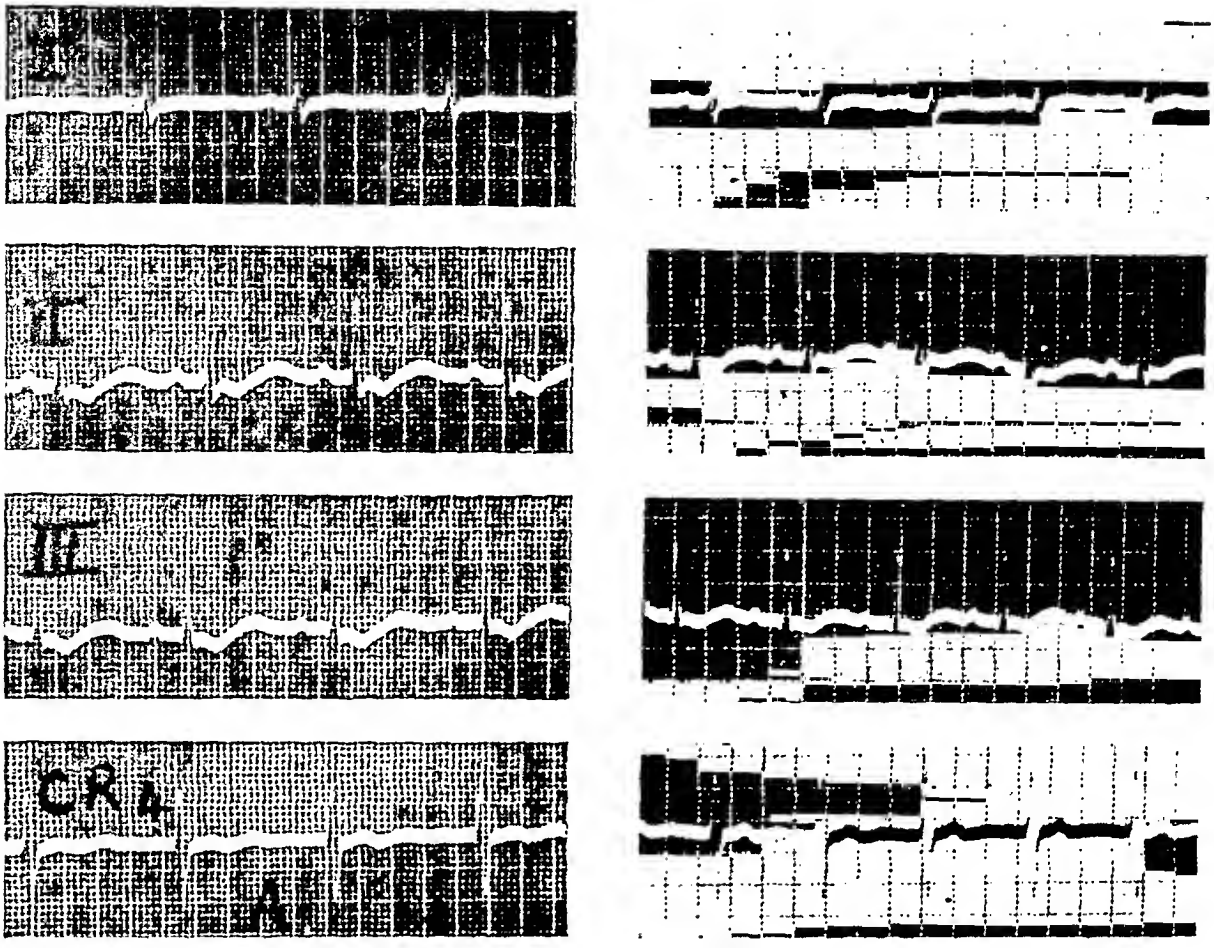

FIG. 2.—Later electrocardiograms of Case 1. (A) 30/4/45. (B) 3/5/45.

pressure was 90/50 and the pulse rate ranged between 100 and 120. There was no œdema and no clinical evidence of vitamin deficiency. Examination of the heart was normal.

Besides the laboratory findings shown on Table I, the urine analysis was normal and a radiogram of the heart showed it to be rather small. The cardiograms are shown in Fig. 5.

On April 27 his clinical condition was worse. He became very weak and developed nausea and vomiting and his blood pressure became unobtainable by the auscultatory method, but was estimated at about 80 mm. systolic by palpation. He was given 2 units of plasma and 1000 c.c. of 5 per cent glucose in normal saline solution. This parenteral treatment was continued daily for four days. By May 2 he was much better and his blood pressure had risen to 120/70. He was then eating well without any more vomiting and his diarrhœa had practically ceased. His improvement after this continued uninterruptedly.

Case 4. Pte. J. B., 25 years old, was captured January 8, 1945 and released April 20, 1945. His story was similar to the others. He was marched for about 25 kilometres a day during the two weeks just before liberation and during this time also suffered from diarrhœa. In addition he gave a story of having had intermittent swelling of the hands and feet and around his eyes from March until shortly before he was admitted. He lost 55 lb. in weight during his confinement. Physical examination except for his emaciation was essentially normal. Examination of his heart revealed normal sounds and no murmurs were heard. The blood pressure was 120/70. There was no œdema and no clinical evidence of vitamin deficiency.

Laboratory findings are shown in Table I. In addition examination of the urine was negative except for a minimal amount of albumin on entry. The plasma albumin was 3·7 and the globulin 1·8 per 100 c.c. on April 26. A radiogram of the heart showed it to be well within normal limits. His cardiograms are shown in Fig. 6.

He ran a temperature for several days ranging from 103 to 104 degrees, with no evidence of any infection. His course in the hospital was uneventful and consisted of steady improvement.

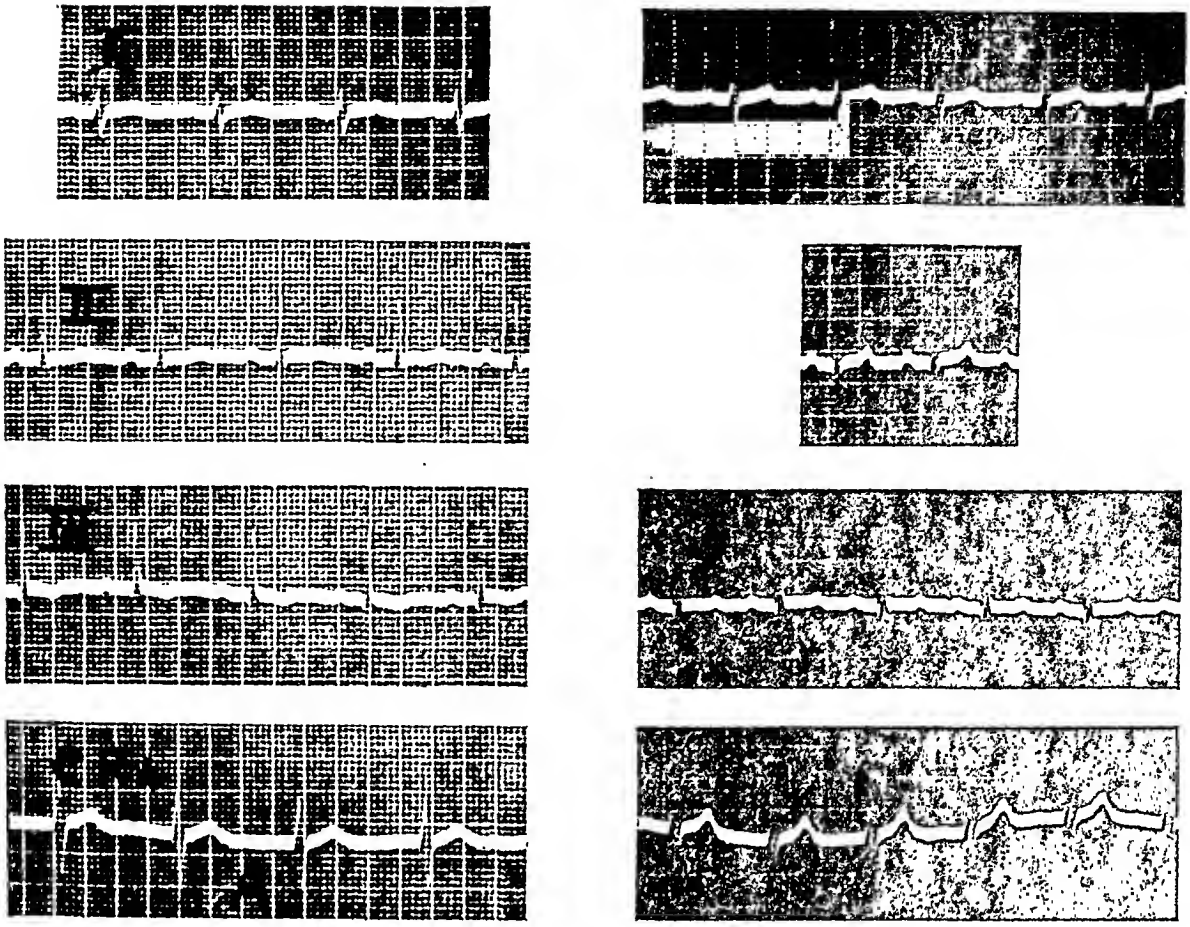

FIG. 3.—Later electrocardiograms of Case 1. (A) 8/5/45. (B) 16/5/45.

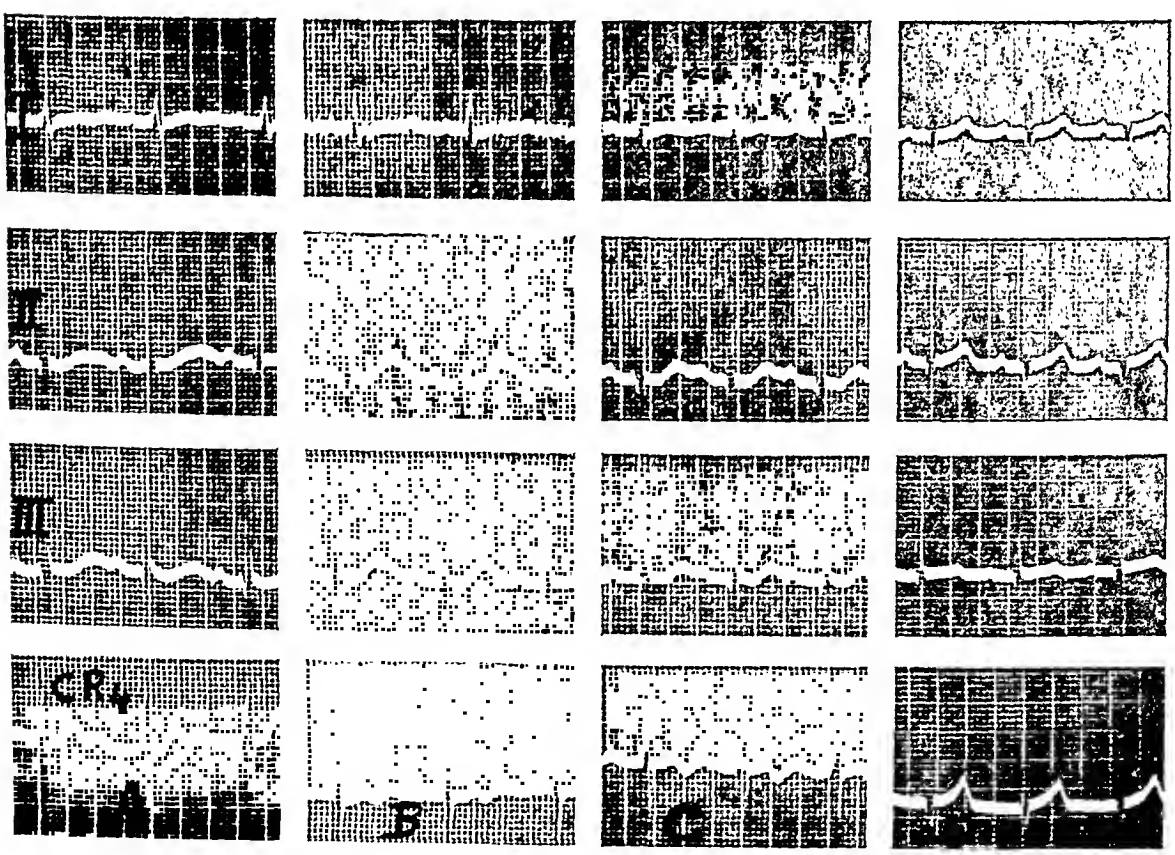

FIG. 4.—Electrocardiograms of Case 2. (A) 25/4/45. (B) 28/4/45. (C) 30/4/45. (D) 8/5/45.

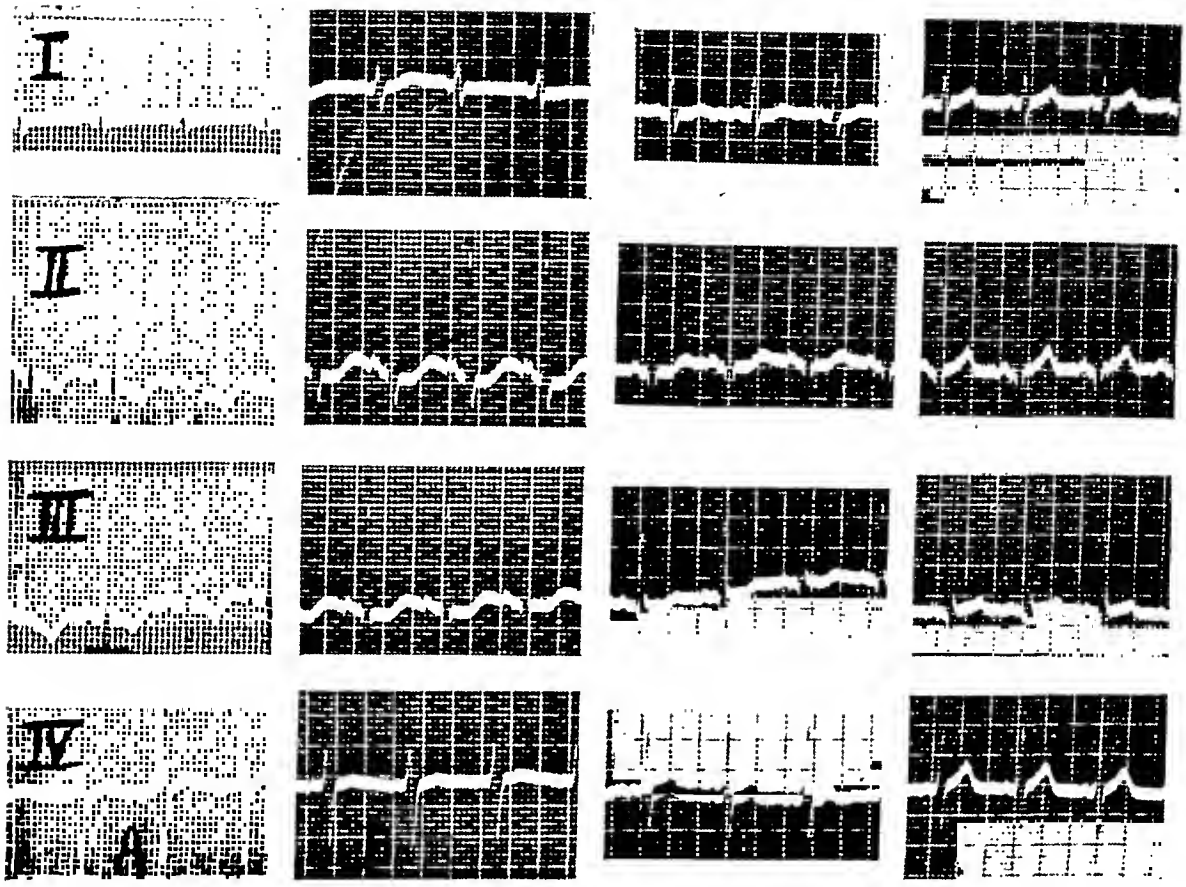

FIG. 5.—Electrocardiograms of Case 3. (A) 29/4/45. (B) 3/5/45. (C) 7/5/45. (D) 16/5/45.

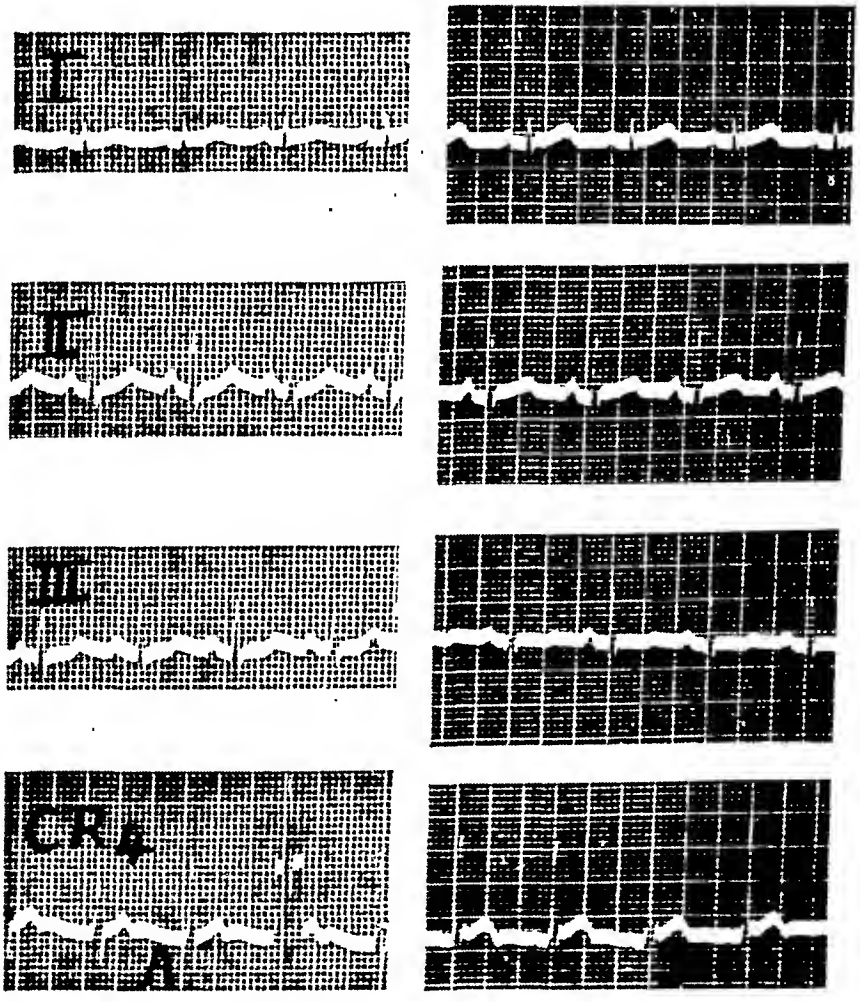

FIG. 6.—Electrocardiograms of Case 4. (A) 26/4/45. (B) 10/5/45.

Comment

The clinical story and physical findings in all four of these patients were essentially the same, varying only in degrees of severity. In no instance was there clinical evidence of vitamin deficiency. All were severely malnourished and dehydrated on admission and were suffering from diarrhœa. No patient had any symptoms or signs of cardiac or peripheral vascular disability, except Case 3, in whom a marked drop in blood pressure and tachycardia developed, accompanied by great weakness, but no other signs of shock. One patient had had moderate intermittent œdema prior to admission but showed none while in the hospital; another developed mild œdema after several days in hospital. In both instances this was considered to be nutritional in origin. In all four cases improvement after the first few days was steady. All showed rather small hearts by roentgenographic examination, and the cardiac findings on physical examination in each were normal. Most of them tended to run a raised temperature without any evidence of infection, which is an extremely common finding among the very undernourished patients. Of interest is the tetany which Case 2 developed without evidence of hypocalcæmia or alkalosis. Treatment other than that described in the case reports consisted of increasing amounts of food by mouth, including milk, eggs, and cereals with an addition of meat after some days. All patients were given 6 multi-vitamin capsules daily which provided a total daily intake of 15,000 U.S.P. units of vitamin A, 1200 U.S.P. units of vitamin D, 6·0 mg. of thiamin chloride, 9·0 mg. of riboflavin, 225 mg. of ascorbic acid, and 60 mg. of nicotinamide. In addition Cases 1 and 3 were given 30 mg. of thiamin and 50 mg. of nicotinamide intramuscularly daily for the first three or four days. (The parenteral nicotinamide was given in relatively small dosage because an adequate supply of this substance was not available at this time.) No digitalis or other specific cardiac medication was given.

Electrocardiographic Findings

The serial cardiograms on the four patients are shown in Fig. 1 to 6. The most striking feature is the unusual T waves. The duration of these deflections, as measured from the initial phase of the QRS complex to the final return to the isoelectric level, is greatly lengthened, and the final phase in all the early records is positive and usually well marked. This may represent a U wave, unusually large in the early tracings, which diminishes or disappears with improvement. The "bifid" T waves occurring in Cases 2 and 4 suggest this as well as the progressive changes in the fourth leads in the other two cases. However, in many of the records it is impossible to say that the entire complex is not T wave. For the sake of convenience and comparison the total duration of this interval has been expressed as the "Q–T interval," In two patients the P–R interval was slightly and inconstantly prolonged; in addition, in Case 1, a widening of the QRS complex occurred.

In all four patients the cardiograms had returned to normal within 14 to 21 days.

Cardiograms were taken in 10 additional severely malnourished soldiers. None had symptoms or signs of cardiovascular disability or of vitamin deficiency.

One showed a prolongation of the Q–T interval of 0·02 sec. above the maximum allowable for normal persons, and low amplitude of all T waves, with a return to normal within one week All other cardiograms were within normal limits.

Discussion

The electrocardiographic abnormalities exhibited by these four patients are unusual and tend to follow a common pattern, the most striking and constant feature being an unusually great prolongation of the Q–T interval or large U waves accompanying abnormal T waves. All of these patients were suffering from severe undernourishment and in addition were dehydrated, as judged from their obvious clinical condition and by the evidence of hæmodilution in Cases 1, 2 and 3, following treatment in the hospital (See Table 1).

None of these patients or any others among more than 400 personally observed showed any clinical evidence of vitamin deficiency. Observers who have studied very large numbers of persons who underwent chronic starvation under similar circumstances in Europe are agreed that clinical vitamin deficiencies are not common (Chapman, Meiklejohn, Pollack, personal communications, 1945).

Cardiographic abnormalities occur in beriberi, which is considered to be due to a lack of thiamin; Weiss and Wilkins (1937) found in a large series of patients studied that such abnormalities were present in 93 per cent of the cases. In 79 per cent the Q–T interval was prolonged beyond the maximum allowed by the Cheer-Li standard (0·38 sec.) and in 45 per cent it was greater than that permitted by the Shepley-Hallaran standard (0·43 sec.). Other changes noted consisted of lowering or inversion of T waves and minor changes in the QRS complexes.

Whether deficiencies in other vitamins lead to alterations in the electrocardiogram is not settled, but it was considered unlikely by Weiss and Wilkins. However, Rachmilewitz and Braun (1944) reported on two patients with severe diarrhœa who were " admitted in a state of severe deficiency." The first showed inversion of the T waves, and the second a well-marked prolongation of the Q–T interval. They attributed this to nicotinic acid deficiency since improvement occurred coincidentally with nicotinic acid administration. Feil (1936) previously had found the Q–T interval to be frequently prolonged in pellagra with a return to normal upon recovery. Usually this shortening of the Q–T interval, which occurred with improvement, ranged from 0·02 to 0·06 sec., but the maximum was 0·12 sec. In addition Feil described inversion of T waves and elevation or depression of the S–T interval as being not uncommon. In neither of these two articles is the possibility excluded that other deficiencies than lack of the pellagra-preventive vitamin complex may have been responsible for the cardiographic findings. Since clinical avitaminosis states are usually associated with multiple deficiencies, particularly as regards the B complex, it is difficult to assess the role that the lack of individual vitamins play in producing the cardiographic abnormalities.

The cardiographic pattern observed in the cases of the present study bears little resemblance to the characteristic changes reported previously in association with avitaminosis. As stated, these patients also had no clinical evidence of the cardiovascular manifestations of beriberi. There was no peripheral vasodilatation, no cardiac enlargement or heart failure, and no polyneuritis. Pellagrous lesions were absent. As Weiss and Wilkins have observed, since the tendency to develop avitaminosis varies directly with metabolic rate, clinical beriberi is not likely to develop in conditions of starvation and inanition.

Although a disturbance of the electrolyte balance of these undernourished patients undoubtedly occurred, it was impossible in this study to investigate this adequately. Hypocalcæmia characteristically produces a prolongation of the Q–T interval which is not uncommonly very marked in degree (Ashman, 1942, and Barker, Johnston, and Wilson, 1937). Other cardiographic changes do not usually develop with low serum calcium levels. None of the four patients studied had a reduction in blood serum calcium values below normal, although it is of interest that Case 2 developed clinical tetany. Since the plasma proteins were not increased it is unlikely that there was an abnormal reduction in the ionized calcium levels.

Pathological and experimental conditions causing abnormalities of the blood potassium produce cardiographic changes. When the potassium level in the blood is increased in man or animals experimentally by the administration of potassium salts (Winkler, *et al.*, 1938, and Chamberlain, *et al.*, 1939) or clinically in renal failure or Addison's disease (Thomson, 1939, and Keith, *et al.*, 1944) the cardiogram first shows an increased height of the T waves especially in the chest lead, with a narrow base and a " peaked " apex. With greater increases in the serum potassium level in experimental animals partial auriculo-ventricular block and intraventricular block occur. The T waves may also be lowered or inverted. The duration of electrical systole was slightly prolonged in three patients in uræmia with high serum potassium studied by Keith *et al.* (1944), but marked alterations in the Q–T intervals did not occur when this was produced experimentally (Chamberlain *et al.*, 1939).

Conversely, in a patient suffering from familial periodic paralysis, reported by Stewart, Smith, and Milhorat (1940), transient abnormalities occurred in the cardiogram when the serum potassium was reduced, consisting of prolonged P–R interval, widened QRS complex, and prolongation of the Q–T interval with a depressed S–T interval and a lowering of T waves.

The cardiograms of the malnourished patients show little in common with the changes occurring with high serum potassium, and the similarities with the abnormalities found in the patient with low blood potassium, although slightly greater, are not at all marked. Whether

such similarity as exists is more than coincidental is merely conjectural since it was impossible to carry out blood potassium studies in these patients.

Post-mortem observations on patients dying of malnutrition (Meiklejohn, 1945, and Pollack, 1945) have revealed that the hearts are small and flabby with brownish pigmentation ; microscopically the muscle fibres show loss of striation. In those cases showing generalized œdema, particularly those who had received fluid and salt for some weeks before death, there was in addition evidence of inter- and intra-fibrillary œdema of the cardiac musculature.

Summary and Conclusions

Case reports are presented on four patients suffering from severe and prolonged malnutrition in whom electrocardiographic abnormalities were observed. These cardiographic changes consisted of a marked prolongation of the Q–T interval, or unusually well-marked, but not persistent U waves, and less constantly, depression of the S–T segment, alterations in T waves, and increase in the P–R and QRS intervals.

Although the available evidence does not permit any certain conclusions to be drawn as to the causation of the cardiographic abnormalities occurring in malnourished persons, it is probable that they represent a composite picture due to prolonged protein and carbohydrate starvation and electrolyte imbalance. There was no evidence of a significant degree of anoxia of the cardiac muscle or of clinical avitaminosis. Vitamin deficiency, however, cannot be entirely ruled out as an ætiological factor in spite of the absence of clinical symptoms and signs. The fact that the cardiograms returned to normal within two to three weeks after the institution of an adequate therapeutic regime suggests that the changes are chiefly due to functional and not to structural causes.

We are indebted to the following for information supplied about the rarity of clinical signs of vitamin deficiency : Dr. A. P. Meiklejohn of U.N.R.R.A. from observations at the Belsen Concentration Camp, Lt.-Col. Herbert Pollack, A.U.S., from observations of liberated prisoners of war, and Dr. Carleton Chapman, U.S.P.H.S. and U.N.R.R.A., from observations in Greece and Jugoslavia : and to the two former for post-mortem observations on patients dying from malnutrition.

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THE EFFECT OF NITRITE AND EXERCISE ON THE INVERTED T WAVE

BY

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Received December 12, 1945

No unequivocal explanation has so far been found of the inverted T wave in the abnormal human electrocardiogram. It is likely that the deformed T wave associated with coronary disease is the outcome of cardiac ischaemia, but this does not appear to explain the mechanism of T-wave inversion in ventricular preponderance where a shift of the heart may play a part. The earlier papers dealing with temporary cardiographic changes in cardiac ischaemia and with the experimental evidence that nitrite increases the blood supply to the myocardium were reviewed by Evans and Hoyle (1933), who studied the effect of nitrite on the inverted T wave. In a series of 23 cases that showed deformity of the T in the form of flattening, diphasic change, or inversion, this component was wholly or partly corrected in 11 following the administration of the vasodilator. They concluded that elevation of the inverted T wave by nitrite in patients with angina pectoris was determined by the relief of myocardial ischaemia, and suggested that further observations might show that the fixed T wave and the one elevated by nitrite had a different significance, and that this might prove to be a measure of the collateral circulation around a damaged portion of heart muscle. Only nine of their cases, however, were of simple cardiac infarction without hypertension or aortic valvular disease, and in only three of these was the T wave corrected by nitrite. Exercising patients with coronary insufficiency will sometimes cause R–T depression or even inversion of the T wave; in others it may correct the deformity. Such changes were considered by Master, Friedman, and Dack (1942), as evidence of coronary abnormality. May (1939) observed that a lowering of the T wave, sometimes with S–T depression, as a result of the oxygen deficiency, gradually induced, is much more common in young athletic subjects than in older people. Levy, Alvan, and Bruenn (1938) agreed that oxygen want caused cardiographic alterations in healthy subjects as well as in patients with heart disease, but showed that the change was far greater when the coronary circulation was impaired. The effect of the administration of oxygen on the cardiogram of cyanosed patients was studied by Edson (1942), who found that the deformed T wave was not always corrected and especially in cases of recent coronary occlusion, while in some depression of the R–T segment or an increase in the degree of inversion of the T wave resulted. An understanding of T-wave changes in relation to myocardial nutrition is still far from complete. An explanation of the altered T wave of ventricular preponderance does not at first sight concern the relief of cardiac ischaemia. In practice, the similarity of the T I type of cardiac infarction and the inversion of T from hypertension or aortic valvular disease is a common problem in differential diagnosis. The chest lead CR_7 of Evans and Hunter (1943) may sometimes assist this differentiation, while the administration of potassium salts (Sharpey-Schafer, 1943) might help if it were a safe method. The following observations on the effects of nitrite and exercise on the inverted T wave were made to evaluate the help that such tests might afford in deciding this common clinical and cardiological problem.

THE INVESTIGATION

Forty-five cases showing deformity of the T wave in their cardiograms were selected for the tests, and were divided into four groups; 16 cases of cardiac infarction (Group I): 13 of

hypertension without clinical evidence of coronary changes (Group II), 9 of cardiac infarction with hypertension (Group III), and 7 cases of aortic valvular disease (Group IV). The criteria adopted in the separation of Groups I and III were a resting blood pressure of 170 mm. systolic at the time of the test or recorded on a previous occasion, and cardiac enlargement on cardioscopy. In Group I, 10 cases of infarction were of the T I type (Parkinson and Bedford, 1928) and 6 of the T III type. Of those cases of infarction with hypertension (Group III), 3 showed cardiographic changes of the T I type and 6 of the T III type. The 20 cases of " left ventricular preponderance " who gave no history of pain that would have been interpreted as indicating coronary disease were made up of 10 cases of simple hypertension, 2 of malignant hypertension, 1 of chronic nephritis with hypertension (Group II), 1 of aortic incompetence, 1 of congenital sub-aortic stenosis, and 5 of aortic stenosis and incompetence (1 rheumatic, 2 atherosclerotic with hypertension, and 2 of syphilitic origin) (Group IV). Eleven of Group II showed changes in the T wave in lead I, as did all the cases in Group IV with the exception of

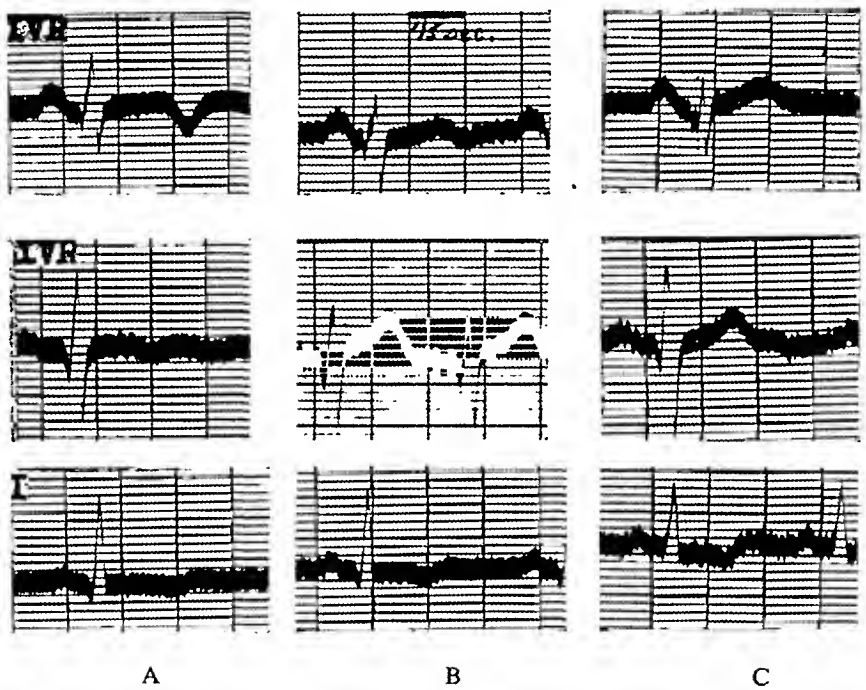

FIG. 1.—The effect of amyl nitrite and of exercise on the deformed T wave of three cases of cardiac infarction. (A) At rest. (B) After nitrite. (C) After exercise.

the patient with a congenital lesion, and in none of them was the inversion of T in IVR greater than in CR_7. At the start of this investigation other leads showing inversion of the T wave were studied, but in most the lead that showed the greatest deformity was selected whether it was lead I, lead II or lead IVR except that lead III was never used.

Nitrite was administered as follows. A capsule of amyl nitrite (5 minims) was broken in a gauze swab below the nose of the patient who was previously reassured as to the safety of the procedure. Four or five deep inhalations were taken. The selected lead was then recorded at half-minute intervals and the blood pressure noted regularly. After an interval, and often on another occasion, glyceryl trinitrate was chewed. Many patients received 3/100 grain, but as a rule a dose of 1/50 or 1/100 grain was taken. Several tracings were then recorded at intervals as well as blood pressure readings.

The exercise test took the form of bending repeatedly to touch the toes, or of raising and lowering the legs with the knees straight while the subject reclined on a couch with the electrodes in position. In order to avoid any influence of drugs, this test was always performed before the administration of the nitrites, and a sufficient interval was allowed between the different procedures for the pulse rate and for the tracing to return to their resting states. Exercise was continued for a few minutes until the patient became fatigued or breathless. Standard exercise tests, such as those devised by Master, Friedman, and Dack (1942) were

not attempted owing to the variable capacity of the subjects. The performance of this test on the couch minimized loss of time before recording the tracing, for Master and his co-workers stated that occasionally the cardiographic changes produced by exercise may disappear within one minute of the cessation of exertion.

Results

In Table I are analysed the effects of nitrite and exercise on the abnormal T wave. Nitrite corrected the deformity in six cases of Group I (37 per cent), in seven of Group II (54 per cent), in two of Group III (22 per cent), and in none of the seven cases of Group IV. In one case

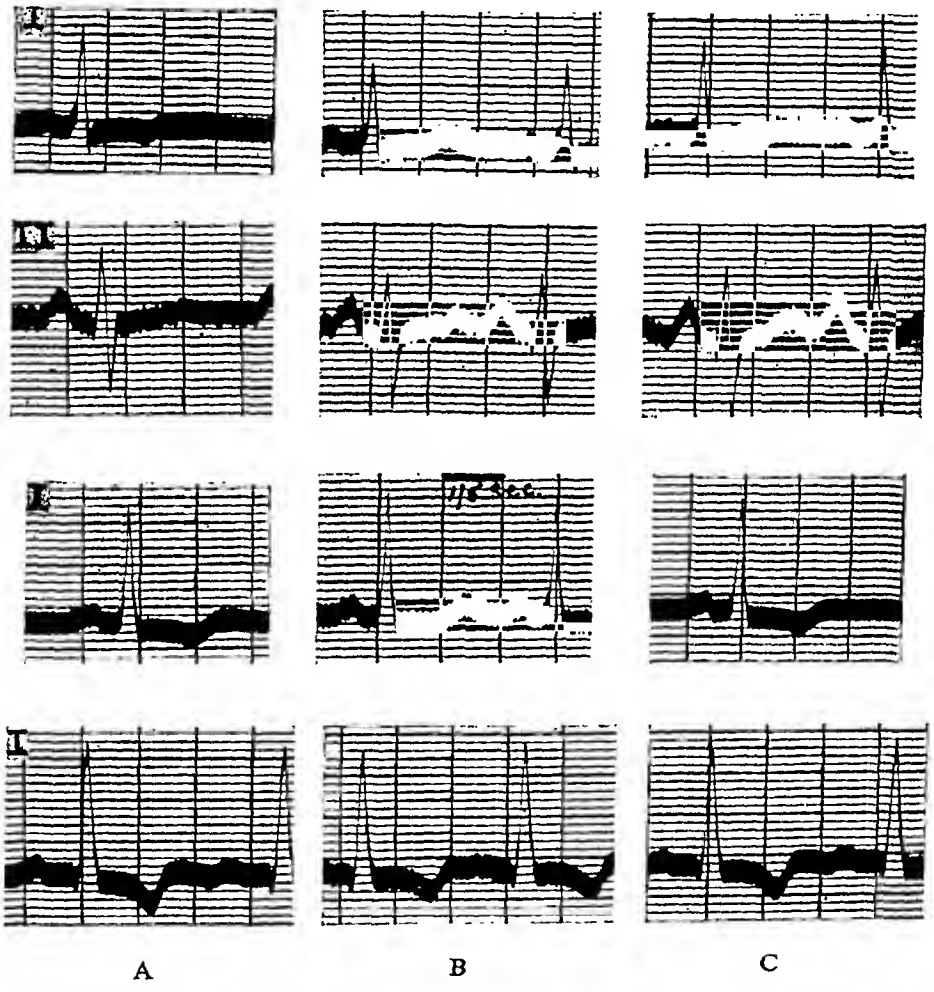

FIG. 2.—The effect of amyl nitrite and of exercise on the deformed T wave of four cases of hypertension. (A) At rest. (B) After nitrite. (C) After exercise.

in each of the first three groups the deformity of the T wave was accentuated. Elevation of this component resulted from exercise in 9 of 16 cases (56 per cent) of simple cardiac infarction (Group I), and in but 2 of the 13 cases (15 per cent) of hypertension without apparent coronary disease (Group II). Of these two, one was a case of benign hypertension, the other of malignant hypertension. Exercise did not alter the T wave in any case of aortic valvular disease (Group IV). No change resulted from nitrite or exercise in four cases of Group I (25 per cent), five of Group II (38 per cent), six of Group III (67 per cent), and seven of Group IV (100 per cent). Only among the cases of cardiac infarction without hypertension (Group I) were found instances of correction of the T wave from exercise but not from nitrite (25 per cent). On the other hand, in Group II five cases showed an elevation with nitrite but not with exercise whereas only one in Group I met with correction from nitrite alone.

TABLE I

THE EFFECTS OF NITRITE AND EXERCISE ON THE ABNORMAL T WAVE

Diagnosis	Effect of Nitrite			Effect of Exercise		
	Deformity corrected	No change	Deformity accentuated	Deformity corrected	No change	Deformity accentuated
Cardiac infarction (16)	6	9	1	9	6	1
Hypertension (13)	7	5	1	2	11	0
Cardiac infarction and hypertension (9)	2	6	1	1	7	1
Aortic valvular disease (7)	0	7	0	0	7	0

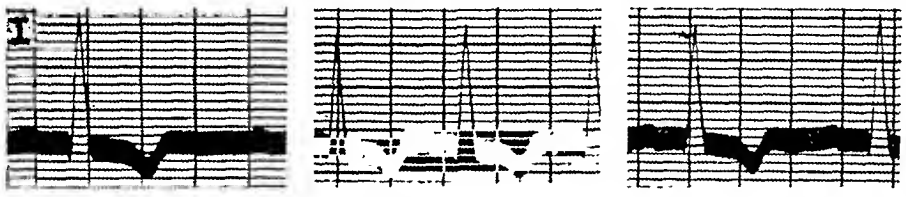

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FIG. 3.—The effect of amyl nitrite and of exercise on the inverted T wave of a case of aortic stenosis with incompetence. (A) At rest. (B) After nitrite. (C) After exercise.

After glyceryl trinitrate, in only 5 of the total 45 cases was any change in the T wave noted, of which 2 received 3/100 gr.; 2, 1/50 gr.; and 1, 1/100 gr., whereas 18 of the cases showed some change after amyl nitrite. These cardiographic changes tended to occur three to five minutes after the patient started to chew the trinitrin and half to one minute after the inhalation of amyl nitrite. The fall of blood pressure after amyl nitrite was swifter, and was generally accompanied by flushing, palpitation, and occasionally faintness, and, although it lasted only one to two minutes, was more dramatic than that which resulted from chewing the tablet. A fall of 30 to 40 mm. pressure was common in cases with resting systolic pressures within normal limits. In subjects with hypertension a fall of 60 to 80 or even 100 mm. was recorded half to one minute after the inhalation, but the original pressure was reached a minute or so later. In few cases, usually those receiving the larger doses of glyceryl trinitrate, there was a corresponding fall of the systolic pressure recorded, and the effect took two to five minutes to develop. Peripheral vasodilatation was less marked, and with the exception of one instance of collapse in an elderly woman who received 3/100 gr., the subjective discomfort was far less. From these results there would appear to be no close association between the fall in blood pressure and the incidence of cardiographic change. Tachycardia was frequent within one minute of amyl nitrite administration, but only a slight increase of pulse rate was noted after trinitrin, presumably because of the factors mentioned, namely, less subjective disturbance and smaller and more gradual fall in blood pressure after the solid preparation. Judging from the results of amyl nitrite administration, there seemed no obvious association between tachycardia and correction of the T wave, as a high pulse rate was noted as frequently with no change in the T wave as in those with an alteration of the complex; there were instances where a case of cardiac infarction, showing correction of the T wave by exercise, failed to show any cardiographic change after nitrite, in spite of a higher heart rate; also, if tachycardia were responsible for this correction, a greater number of cases might be expected to show it after exercise in Group II. Although exercise in most cases caused an increase in the blood pressure (e.g. 150/120 to 195/140, 140/90 to 180/100, and 250/120 to 280/140) there seemed no relation between the degree or frequency of changes in the blood pressure and cardiographic records in any group.

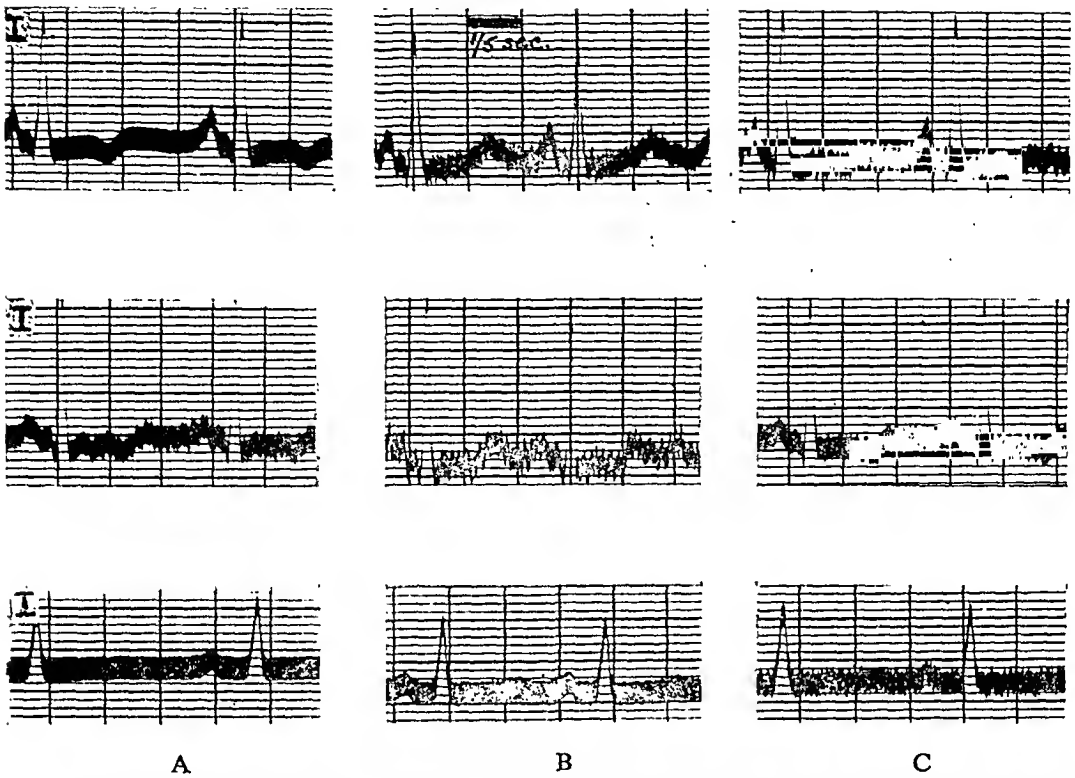
Changes in the R–T segment were also noted, although only T wave alterations have been mentioned. In three cases of cardiac infarction R–T depression occurred with exercise but the T wave became taller, and in another the T wave was unchanged in spite of slight R–T depression.

Discussion

The present results with nitrite are comparable with those obtained by Evans and Hoyle (1933); 18 of a total of 45 cases showed a change in the T wave after administration of the vasodilator, whereas the figures of the previous observers were 11 of 23 cases. In the present series, in 6 of the 16 cases of cardiac infarction in Group I the deformity was corrected whereas the comparable figures in the 1933 publication were 3 out of 9 cases. Turning to Group II one finds a more frequent change in the T wave after amyl nitrite in cases of hypertension without apparent coronary lesions than in those with infarction. In 7 of the 13 cases the T wave was corrected in Group II (54 per cent) compared with 6 of 16 cases in Group I (37 per cent). If the cases of left ventricular preponderance including hypertension and aortic valvular disease (Groups II and IV) were not separated, the figures for correction by nitrite would be closer (35 per cent for Group II + Group IV). The effect of nitrite, therefore, cannot serve usefully in differentiating the cardiogram of cardiac infarction from that of left ventricular preponderance. The elucidation of cardiographic changes of the T I type occurring with hypertension and coronary pain must depend as yet on the history and on the clinical findings, while some help may be obtained from the chest lead CR_7 of Evans and Hunter.

If the relief of myocardial ischaemia is the only factor determining correction of the deformed T wave of infarction, difficulty arises in the explanation of similar cardiographic changes after exercise. An increase in the general circulation rate will lead to a greater coronary circulation rate unless the vessels are completely occluded (Peel, 1943). It is a well-known fact that patients with angina are sometimes hindered by pain at the start of a walk, but after a short distance may gain their "second wind" and complete the journey without further interruption. Anginal pain, however, accompanied the elevation of the T wave in four cases of this series, which fact does not conform to the theory of improved coronary flow with a certain amount of exertion. There is no doubt that both amyl nitrite and glyceryl trinitrate cause dilation of the coronary arteries and that these drugs will prevent the pain and also the associated R–T depression or T wave inversion, produced by exercise in some patients with angina. It is difficult to explain why glyceryl trinitrate, generally considered as powerful an antispasmodic as amyl nitrite, if not so prompt in action, does not produce comparable correction of the inverted T wave. The possibility that tachycardia induced by the volatile drug and by exercise, might influence this cardiographic alteration has already been discussed with cautious disbelief. These conclusions are in agreement with those of Evans and Hoyle.

As regards the cardiogram of left ventricular preponderance, the characteristic changes, including T-wave inversion, are presumed to depend on the anatomical configuration of the cardiac chambers in relation to each other and to the chest as a whole, and not on the condition of the heart muscle (Master, 1942). Myocardial ischaemia is not considered to be a factor. One may next look to a change in posture of the heart to explain the correction by nitrite of the hypertensive T wave deformity. A recent claim by Goldberger (1945), that such changes are similar, if not identical, with those produced by deep inspiration, requires consideration. Goldberger associates this correction with rotation of the heart and suggests that, although other factors may take part, this same mechanism underlies the effects of nitrite. The heart, which according to Scherf and Zdansky (1929) decreases in size following inhalation of this drug, is assumed by Goldberger to lie more vertically, and thus rotation would occur as in the assumption of the upright posture with deep inspiration. Hyperventilation was also often observed after amyl nitrite inhalation. From a comparison of the changes induced in the inverted T wave by deep inspiration in the upright position with those due to amyl nitrite, it would appear that the alteration of cardiac posture must play little if any part in the effects of the vasodilator (Fig. 4). Four cases of infarction and seven of hypertension were tested for such effects. When the selected lead (lead I in ten cases, lead II in one case) had been recorded with the patient lying flat, it was repeated in the upright posture during deep inspiration. Amyl nitrite was subsequently administered with the subject in the reclining position so that the effect of the vasodilator on the cardiogram could be compared with that of cardiac tilt. Only in one of the four cases of cardiac infarction and in two of the seven cases of hypertension so tested, did postural change with depression of the diaphragm cause a very slight correction of the deformed T wave. The effect of amyl nitrite on the size of the heart needs to be confirmed, but my results from varying the posture of patients with deformity of the T wave in



A B C

FIG. 4.—The effect of amyl nitrite and of deep inspiration in the upright posture on the deformed T wave of two cases of hypertension and one of anterior cardiac infarction. (A) Supine. (B) After nitrite. (C) Upright inspiration.

the cardiogram are not in agreement with those of Goldberger. Meanwhile, no satisfactory explanation is forthcoming for the correction by nitrite of the inverted T wave of hypertension.

SUMMARY AND CONCLUSIONS

The effect of nitrite and of exercise on the inverted or depressed T wave of the cardiogram was studied in 45 patients. These were divided into four groups. Group I consisted of 16 cases of cardiac infarction without hypertension, Group II of 13 cases of hypertension without clinical evidence of coronary disease, Group III of 9 cases of infarction with hypertension, and Group IV of 7 cases of aortic valvular disease.

Inhalation of amyl nitrite will often correct the inverted T wave of the cardiogram in cardiac infarction (6 of 16 cases). As often it will correct the deformed T wave of hypertension (7 of 13 cases) but no such changes resulted in any of the 7 cases of aortic valvular disease.

Exercise will give similar results in that it righted the deformed T wave in 9 of 16 patient with cardiac infarction, and in 2 of the 13 with hypertension; in none of the 7 with aortic valvular disease was there any change.

In 11 cases the T wave of the cardiogram taken when the patient was in the upright posture, with the diaphragm depressed by deep inspiration, was seldom different from the tracing in the supine posture on quiet respiration.

It is not even certain that the corrected T wave from nitrite inhalation and exercise is brought about by the relief of myocardial ischaemia since the deformed T wave of hypertension responds in the same way. Tachycardia and variation in blood pressure and of posture seem to play no part in such correction.

The tests of amyl nitrite inhalation, exercise, and change of posture will not assist in differentiating the cardiographic pattern of cardiac infarction from that of hypertension.

I am indebted to Dr. William Evans for his advice, and to Dr. E. Miles, Medical Superintendent of Oldchurch Hospital, for facilities for this investigation.

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AURICULAR PREMATURE SYSTOLES: THE DURATION OF THE ELECTRICAL SYSTOLE

BY

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Received November 10, 1945

In a recent electrocardiographic investigation (Berliner and Lewithin, 1945) the aberration of the ventricular complex of auricular premature systoles (*APS*)* was studied. Variations in amplitude, duration, direction, and configuration were found and described in detail. In the course of that investigation, a new feature of the *APS*, shortening of the electrical systole (Q–T interval), was discovered. This subject has since been studied by careful measurements which are reported in the present paper.

Material and Method

We used 100 electrocardiograms of different patients in this study, selected from the records of over 250 patients exhibiting *APS*. The selection was made on the basis of technical qualities of the tracings. We chose only clear records in which the exact end-points of the T waves were easily discernible. Tracings blurred by muscle tremor or technical defects were eliminated; as were such perfect records in which low amplitude of the T waves made accurate measurement of the Q–T interval impossible; and also all those records in which the *APS* were found to occur at the beginning of a tracing or at its very end (with the exception of Fig. 2A). Records with inverted T waves were purposely included.

Of the four leads available in practically all cases, we selected that lead in which the end-points of the T waves were most distinct, and analyzed one *APS* of that lead. The degree of prematurity of this *APS* and the degree of its aberration were determined first, and for this purpose the criteria established in the previous study were again used. Measurements were then made on five successive heart beats, the two beats preceding the *APS*, the *APS* itself, and the two beats following it. All measurements were made with the aid of a magnifying glass. The duration of QRS and RS–T † was measured in each of the five beats. The Q–T intervals were then obtained by adding up the values for QRS and RS–T. In the normal beat just preceding the *APS*, however, RS–T and Q–T could usually not be measured because the P wave of the *APS* was superimposed on its T wave. That was the reason why the beat preceding it was also measured and was chosen as *the* normal for purposes of comparison. QRS, RS–T, and Q–T of the *APS* were compared with the respective intervals of the normal beat and the post-extrasystolic beat. Examples are given in the legend to Fig. 1.

Results

QRS duration and Q–T interval. In 47 of our 100 *APS*, the duration of QRS did not differ from that of the normal beats or the difference was too minute for measurement. In 23, QRS duration was shortened; this shortening never exceeded 0·02 second. In 30 the QRS complexes were prolonged. The prolongation was marked (0·02 second or more) in 15 of these. Marked prolongation was usually associated with other features of aberration, viz.

* *APS* will be used as an abbreviation for auricular premature systole(s) throughout this paper.

† By RS–T interval we mean the interval beginning at the RS–T junction and ending at the end of the T wave.

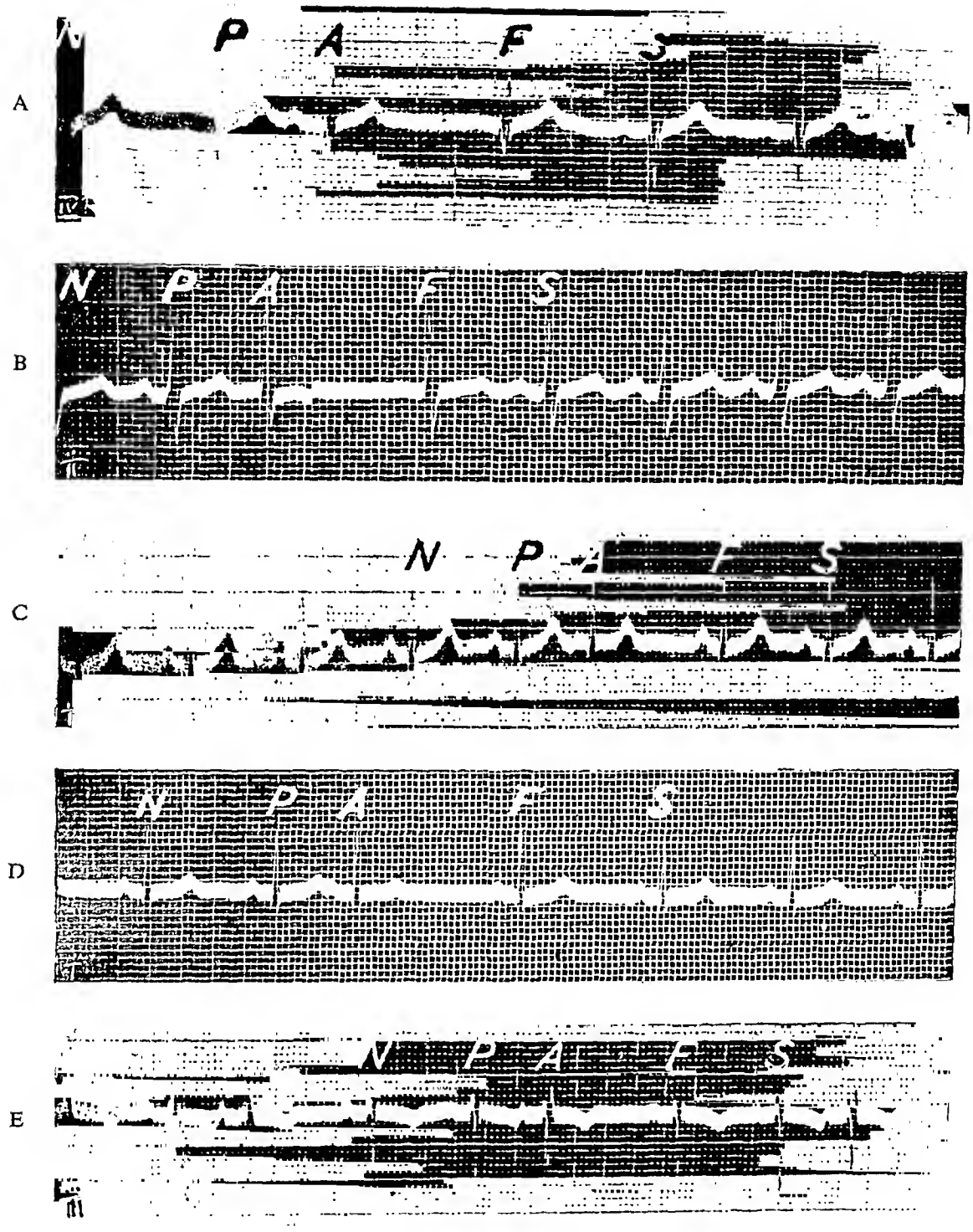

FIG. 1.—Shortening of the electrical systole in auricular premature systoles (*APS*)—five typical examples. QRS duration essentially unchanged, RS–T duration (from the RS–T junction to the end of *T*) shortened. N, normal beat; P, beat preceding the *APS*; A, *APS*; F, beat following the *APS*; S, subsequent beat. Measurements in seconds:

(A)	QRS	RS–T	Q–T
N	0·075	0·275	0·350
P	0·075	0·275	0·350
A	0·075	0·260	0·335
F	0·080	0·285	0·365
S	0·080	0·280	0·360

(B)	QRS	RS–T	Q–T
N	cut off	0·28	×
P	0·085	×	×
A	0·085	0·26	0·345
F	0·080	0·29	0·370
S	0·095	0·28	0·375

(C)	QRS	RS–T	Q–T
N	0·07	0·30	0·37
P	0·075	×	×
A	0·07	0·29	0·36
F	0·07	0·32	0·39
S	0·07	0·30	0·37

(D)	QRS	RS–T	Q–T
N	0·07	0·31	0·38
P	0·065	×	×
A	0·07	0·28	0·35
F	0·07	0·32	0·39
S	0·065	0·32	0·385

(E)	QRS	RS–T	Q–T
N	0·07	0·32	0·39
P	0·07	×	×
A	0·07	0·25	0·32
F	0·07	0·31	0·38
S	0·07	×	×

changes in amplitude, configuration, or direction. When we measured the duration of RS–T in the 15 *APS* which showed marked prolongation of QRS, we often found marked shortening of RS–T. So great was the shortening of RS–T in 9 of these 15 cases, that it " compensated " for the increase in QRS duration, making the total Q–T interval of the *APS* equal to the Q–T interval of the normal beats or even shorter. An example will illustrate this point (Fig. 3A, compare A with N).

QRS of *APS* (A) prolonged by	0·05 second
RS–T of *APS* (A) shortened by	0·06 second
Q–T interval of *APS* (A) shortened by	0·01 second

Our measurements of the QRS duration of *APS* may be summed up by the statement that changes in QRS duration did not significantly affect the Q–T interval of the *APS*.

Measurements of RS–T. The Q–T interval of an *APS* is usually shortened. This shortening occurs in the RS–T interval. When the RS–T interval of the *APS* was compared with that of the normal beat (N), it was found shortened in 82 per cent of the cases (Fig. 1). In 12 per cent there was no difference in RS–T duration, and in only 6 per cent was there a slight prolongation (Fig. 2).

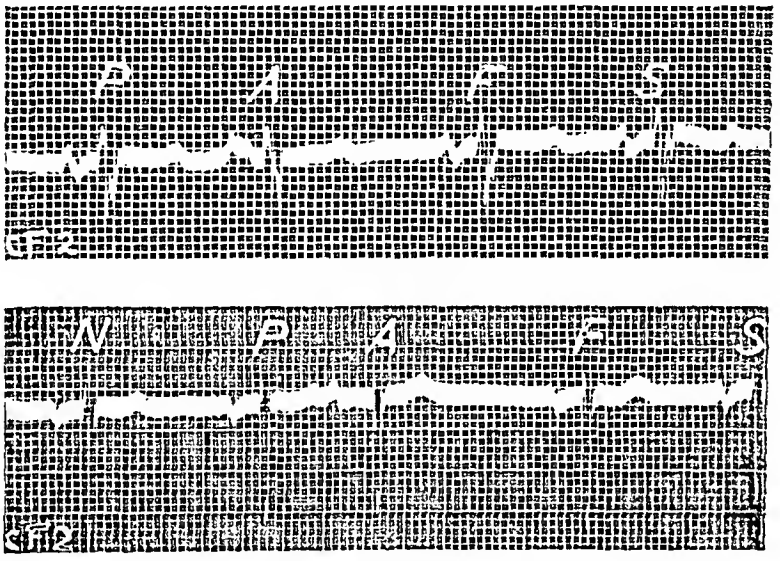

FIG. 2.—Slight lengthening of the electrical systole in auricular premature systoles (*APS*)—two examples of an unusual condition. QRS duration essentially unchanged, RS–T duration (from the RS–T junction to the end of T) lengthened. N, normal beat; P, beat preceding the *APS*; A, *APS*; F, beat following the *APS*; S, subsequent beat. Measurements in seconds.

(A)

	QRS	RS–T	Q–T
N		cut off	
P	0·095	0·325	0·42
A	0·09	0·33	0·42
F	0·095	0·33	0·425
S	0·10	0·32	0·42

(B)

	QRS	RS–T	Q–T
N	0·07	0·26	0·33
P	0·08	0·26	0·34
A	0·08	0·27	0·35
F	0·07	0·29	0·36
S		cut off	

We were unable to discover what causes the shortening of RS–T in the *APS*. Various possible factors were investigated. The effect of T-wave inversion was easily ruled out. Leads in which all T waves or only the T waves of the *APS* were inverted showed no more shortening than leads in which they were upright. We then studied the effect which the degree of prematurity of an *APS* might have on its RS–T duration. For this purpose, we compared the RS–T intervals of early and late *APS*. Our series included 15 early *APS*; their P waves were superimposed on the ascending limb of the preceding T wave (" location 4 " of the previous paper). Our series also included 23 late *APS* the P waves of which did not touch the preceding T waves (" location 1 " of the previous paper). Shortening of RS–T was no more marked in the early *APS* than in the late ones, and the frequency of RS–T shortening was the same in

both groups (Table I). We concluded that the degree of prematurity of an *APS* has no influence on the duration of its RS–T interval.

TABLE I.—Comparison of Early and Late Auricular Premature Systoles (*APS*)

	Number over of cases	RS–T interval shorter than normal	RS–T interval identical with normal beats	RS–T interval longer than normal	Shortening of RS–T varied
Early *APS* (location 4)	15	13	0	2	From 0·01 to 0·07 second.
Late *APS* (location 1)	23	19	3	1	From 0·005 to 0·06 second.

Another possible factor investigated by us was the degree of aberration, but it too was ruled out. *APS* with aberration showed no more shortening of RS–T than *APS* without any aberration. One group of markedly aberrant *APS*, however, formed an exception, viz. *APS* with marked prolongation of their QRS complexes. As mentioned above, in most of these *APS* (9 out of 15 cases) prolongation of QRS was accompanied by an extra marked shortening of RS–T. At times, this shortening of RS–T was so marked that it overbalanced the prolongation of QRS; the duration of Q–T was then shorter than that of the normal beats (Fig. 3A). The highest degrees of RS–T shortening, by as much as 0·06 and 0·07 sec., occurred in

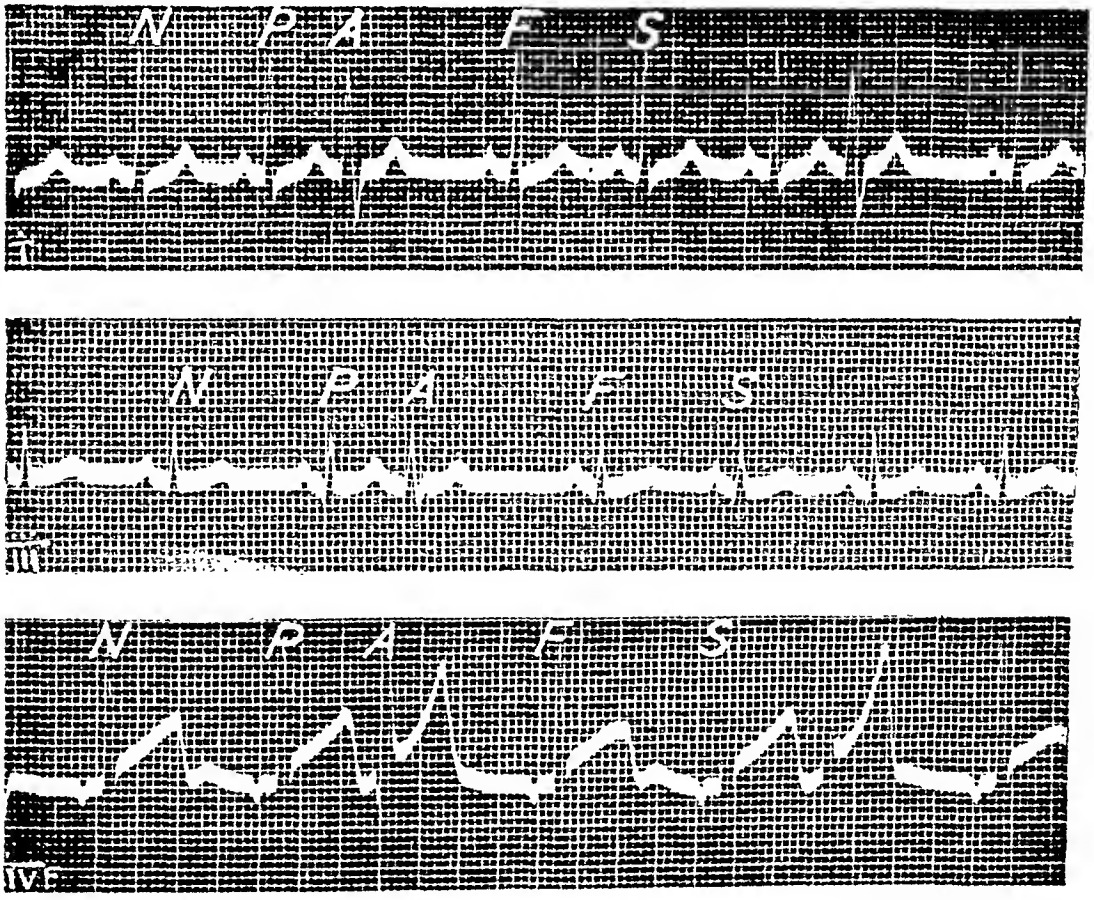

Fig. 3.—Auricular premature systoles (*APS*) showing increased QRS duration but markedly decreased RS–T duration—three examples. N, normal beat; P, beat preceding the *APS*; A, *APS*; F, beat following the *APS*; S, subsequent beat. Measurements in seconds.

(A)	QRS	RS–T	Q–T
N	0·08	0·31	0·39
P	0·08	×	×
A	0·13	0·25	0·38
F	0·09	0·31	0·40
S	0·08	0·31	0·39

(B)	QRS	RS–T	Q–T
N	0·06	0·28	0·34
P	0·07	×	
A	0·12	0·23	0·35
F	0·07	0·29	0·36
S	0·07	0·29	0·36

(C)	QRS	RS–T	Q–T
N	0·065	0·37	0·435
P	0·07	×	×
A	0·10	0·34	0·44
F	0·07	0·38	0·45
S	0·07	×	×

such *APS* with markedly prolonged QRS complexes. This may be more than a coincidence; in fact, it suggests a possible interdependence of QRS and RS–T. There were, on the other hand, 3 cases in which such "compensation" did not take place; both the QRS and the RS–T intervals were prolonged, resulting in marked prolongation of Q–T, up to 0·12 sec. (Fig. 4A and Table II).

TABLE II

AURICULAR PREMATURE SYSTOLES (*APS*) WITH MARKED INCREASE IN QRS DURATION. (Measurements in seconds.)

	QRS duration increased by	RS–T duration shortened by	RS–T duration lengthened by	Resulting Q–T compared to normal	Illustrated in
1	0·02	0·04	—	−0·02	
2	0·02	0·04	—	−0·02	
3	0·02	0·02	—	identical	
4	0·02	0·01	—	+0·01	
5	0·03	0·03	—	identical	Fig. 3C
6	0·03	0·03	—	identical	
7	0·03	0·02	—	+0·01	
8	0·03	0·01	—	+0·02	
9	0·03	—	0·01	+0·04	
10	0·04	0·04	—	identical	
11	0·04	—	0·035	+0·075	Fig. 4A
12	0·04	—	0·08	+0·12	Fig. 4B
13	0·05	0·06	—	−0·01	Fig. 3A
14	0·05	0·05	—	identical	
15	0·06	0·05	—	+0·01	Fig. 3B

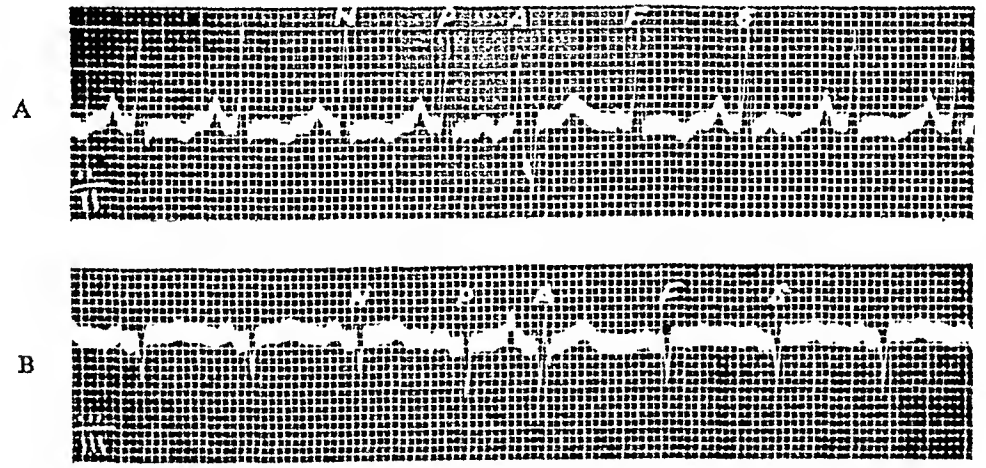

FIG. 4.—Auricular premature systoles (*APS*) showing increased duration of both QRS and RS–T—two examples. N, normal beat; P, beat preceding the *APS*; A, *APS*; F, beat following the *APS*; S, subsequent beat. Measurements in seconds.

(A)

	QRS	RS–T	Q–T
N	0·08	0·24	0·32
P	0·085	×	×
A	0·12	0·32	0·44
F	0·08	0·26	0·34
S	0·08	0·25	0·33

(B)

	QRS	RS–T	Q–T
N	0·06	0·225	0·285
P	0·055	×	×
A	0·10	0·26	0·36
F	0·06	0·23	0·29
S	0·07	0·22	0·29

Comparison of APS *with the following beat.* The beat following an *APS* has a prolonged RS–T interval. When we compared the post-extrasystolic beat with the *APS*, the RS–T prolongation of the former was a practically constant finding. But even when we compared the post-extrasystolic beat with the normal beat N, prolongation of RS–T was found in a high percentage of cases (Table III). The prolongation usually amounted to 0·01 to 0·02 sec., but greater prolongation, of 0·06, 0·07, and even 0·08 sec. occurred occasionally. The effect of

the pause was obvious. In general, the longer the pause after an *APS*, the greater was the prolongation of the RS–T interval of the following beat; but this relationship was by no means consistent, and actual shortening of the RS–T interval of the following beat occasionally occurred, even after a long pause.

TABLE III

COMPARISON OF POST-EXTRASYSTOLIC BEAT (F) WITH AURICULAR PREMATURE SYSTOLE (*APS*) AND WITH NORMAL BEAT (N)

	RS–T longer (per cent)	RS–T identical (per cent)	RS–T shorter (per cent)
F compared with *APS* ..	97	1	2
F compared with N	68	22	10

COMMENT

Our investigation has established two facts: The RS–T interval (and thereby the Q–T interval) of an auricular premature systole is shortened, that of the post-extrasystolic beat is lengthened. Shortening of the electrical systole is a feature of auricular premature systoles not heretofore known, and its significance is not yet understood. Observations on the Q–T interval of normal beats were published by us (Berliner, 1931). Since then, knowledge of this subject has not materially increased. Varied factors, e.g. blood calcium level and digitalis, are known to influence the Q–T interval of normal beats but the determining factor unquestionably is the heart rate. The Q–T interval is shorter for faster rates and longer for slower rates. The relationship of heart rate and Q–T interval is expressed by Bazett's formula (1920)

$$Q\text{–}T = K \cdot \sqrt{\text{cycle length}},$$

the constant K being 0·37 for men and 0·40 for women. This formula or any of its variants obviously applies to beats occurring in regular rhythm and cannot be used to predict the Q–T interval of premature beats. It was, therefore, not employed in the present study. Rate or cycle length may, however, still be found to have an influence on the Q–T interval of premature beats and post-extrasystolic beats. Following the post-extrasystolic pause we found the Q–T interval lengthened. There, at least, the influence of cycle length appears very probable.

We were unable to find out what causes the variations of RS–T duration discovered by us. We may, however, have a clue in the contrast between shortened RS–T in the *APS* and lengthened RS–T in the post-extrasystolic beats. In a separate investigation of ventricular premature systoles, which will be reported later, we found exactly the same conditions; the RS–T intervals of ventricular premature beats are also shorter than those of normal beats (irrespective of the large size of the T waves), and the RS–T intervals of the post-extrasystolic beats are longer. It seems most likely to us that the shortening of RS–T in all premature systoles is caused by their prematurity. Prematurity results in incomplete diastolic filling of the ventricles, and this may be reflected in a shorter duration of RS–T. The post-extrasystolic pause, on the other hand, leads to greater diastolic filling of the ventricles, and this may give rise to an increased RS–T duration. Should this assumption be proved correct, we might be brought nearer to the solution of a basic electrocardiographic problem. The significance of RS–T interval variations in *normal* beats has always been obscure. It might then be found that they too are caused by changes in the diastolic filling of the ventricles.

In conclusion, a remark about measurements of Q–T intervals in general may be in order. Our findings clearly show that the QRS and RS–T intervals vary separately and perhaps independently. They should, therefore, be studied separately. Albers and Bedbur (1941) did that and found that the duration of QRS depends on the heart rate, the duration of RS–T on the heart rate, the age of the patient, and the degree of axis deviation. It was mentioned before that we repeatedly found prolongation of QRS associated with marked shortening of RS–T; the resulting Q–T interval was normal or nearly normal (Fig. 3). Simple measurements of Q–T in such cases would not have revealed the marked shortening of RS–T. Our

experience, therefore, convinces us that measurements of Q–T alone are insufficient and should be replaced by separate measurements of QRS and RS–T.

Summary and Conclusions

The duration of QRS and RS–T of 100 auricular premature systoles (*APS*) was measured and two facts were established: (1) the RS–T interval of an *APS* is usually shorter than that of normal beats, and (2) the RS–T interval of the post-extrasystolic beat is lengthened.

The greatest degrees of shortening of RS–T were found in *APS* with marked widening of their QRS complexes. As a result, the Q–T interval of these *APS* was no longer than that of the normal beats.

QRS and RS–T intervals of *APS* vary independently and should be studied separately. Simple measurements of Q–T intervals are insufficient.

Shortening of RS–T in *APS* is probably caused by the incomplete diastolic filling of the ventricles resulting from prematurity, while lengthening of RS–T in post-extrasystolic beats is probably caused by greater diastolic filling.

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PULMONARY VASCULAR SCLEROSIS WITH RIGHT VENTRICULAR FAILURE

BY

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Received December 19, 1945

The following is an account of a patient with pulmonary vascular sclerosis who died of right ventricular failure within four months of the appearance of the first symptom of ill health.

A navvy charge hand, aged 34, was admitted to Addenbrooke's Hospital on November 6, 1942. In August 1942 he noticed that some of his teeth were very loose and tended to bleed easily, and shortly after this that he was breathless on exertion. Until then he had always been fit with no cough or breathlessness. In early October he went to the dentist, and twelve teeth were extracted under general anæsthesia. Following these extractions breathlessness on exertion gradually increased so that when he was admitted to hospital he could walk up six steps only with difficulty. A week before admission he had also noticed slight swelling of his left leg, occasional palpitation, and some upper abdominal pain and flatulence after food. His appetite remained good and his weight constant. His work had not been physically very strenuous but his hours had been long—from eight in the morning sometimes until midnight. As this was seven miles from home he used to cycle to and fro. He often worked a seven-day week.

In the past he had had no serious illnesses, no rheumatism, nor rheumatic fever, nor other condition that might predispose to cardiac trouble. He had been accustomed to smoke up to 50 cigarettes a day and drank a moderate amount of beer but no spirits. His family history was healthy and did not suggest any tendency to arteriosclerosis or cardiac disease. His mother and father and brothers and sisters were all alive and well.

On admission he was very breathless and slightly cyanosed. The pulse was regular—rate 100. Blood pressure 140/90, respiratory rate 20, temperature normal. A teleradiogram showed that the heart was enlarged (15·3 cm. in the transverse diameter) with marked bulging of the pulmonary artery (Fig. 1). The cardiogram showed right axis deviation with inversion of T II and T III (Fig. 2). The heart sounds were poor in quality with gallop rhythm and the pulmonary second sound was accentuated. There were no murmurs, clubbing of the fingers, venous pulsation, nor œdema, and no evidence of arteriosclerosis in the radial, brachial, or retinal arteries. The respiratory movements were good and there were no signs of chronic bronchitis or emphysema; a few crepitations were audible at the right base.

The liver appeared congested, the edge being palpable two inches below the costal margin. There was no abdominal tenderness and no evidence of ascites. The remaining teeth appeared healthy and the gums had healed well following extraction. The urine contained a trace of albumin, but was otherwise normal.

Blood count showed 5·6 million red corpuscles with hæmoglobin 112 per cent and 12,800 leucocytes with a normal differential count. Blood culture was sterile and the Wasserman reaction of the blood was negative. Blood urea 37 mg. per 100 c.c. Blood sedimentation rate on two occasions 1 and 4 mm. per hour respectively.

Progress. In spite of treatment by rest and full digitilization, progress was steadily downhill from the day of admission until death on December 2, 1942. During this period there was practically no change in either the pulse rate or the respiratory rate. Breathlessness and distress on the slightest exertion became progressively more marked and cyanosis steadily increased.

Post-mortem Examination

Congestion of the lungs, the lower lobes being tough and slightly nodular in consistency and the cut surface of the anterior borders yellowish-grey in colour, with many small rusty-red patches. Considerable emphysema of anterior borders only, without noticeable distention of the lung or formation of bullæ. One small fragment of ante-mortem thrombus in a small pulmonary artery in the right lower lobe, the area supplied by this vessel being hyperæmic but not infarcted. Unusually conspicuous blood vessels everywhere on the cut surfaces of the lungs. Conspicuous atheroma of main pulmonary artery and all its larger branches. Pulmonary veins normal. Only slight atheroma of aorta and its branches, almost none of coronary arteries. Slight excess (about 50 c.c.) of clear yellow fluid in

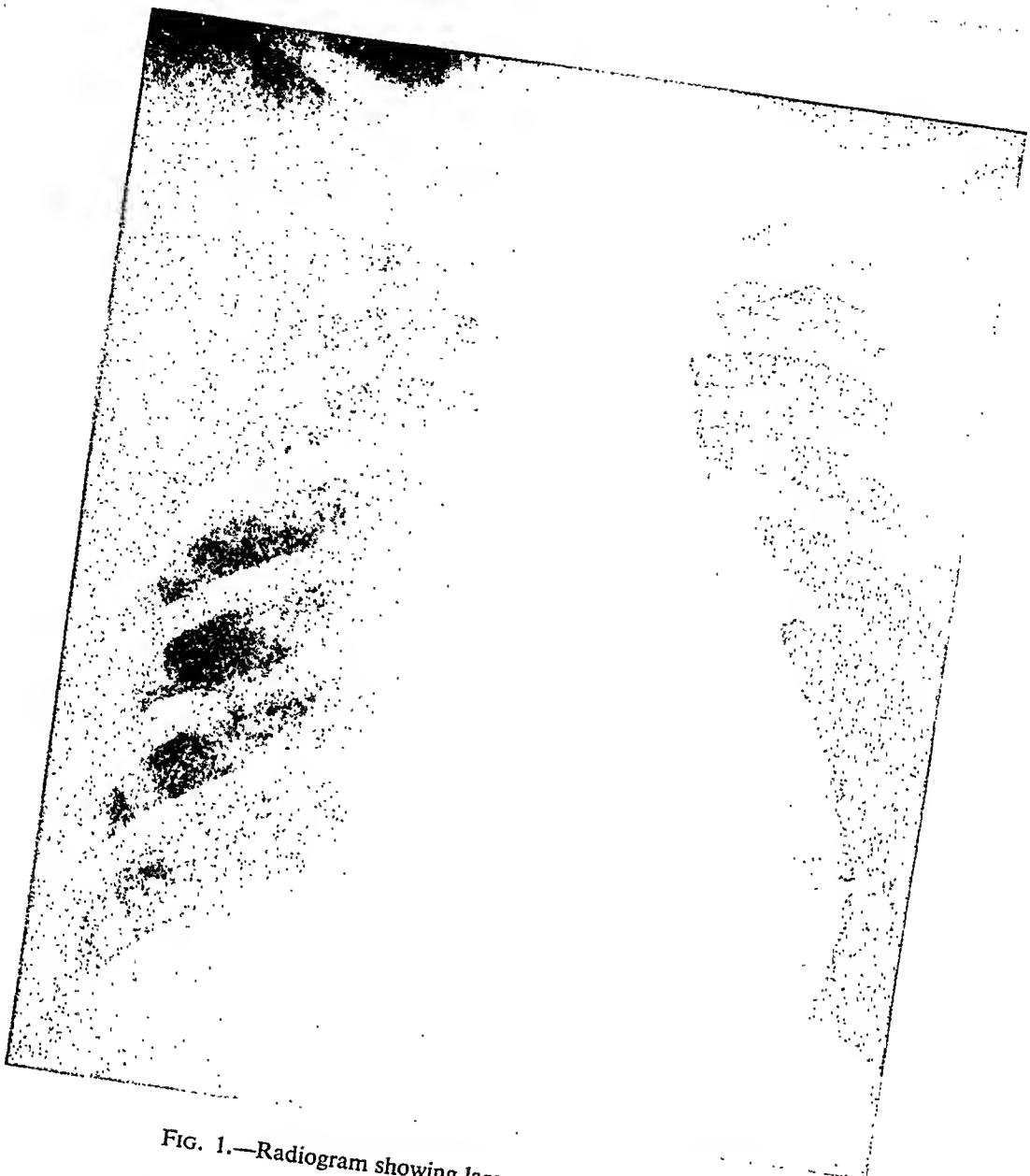

FIG. 1.—Radiogram showing large pulmonary artery.

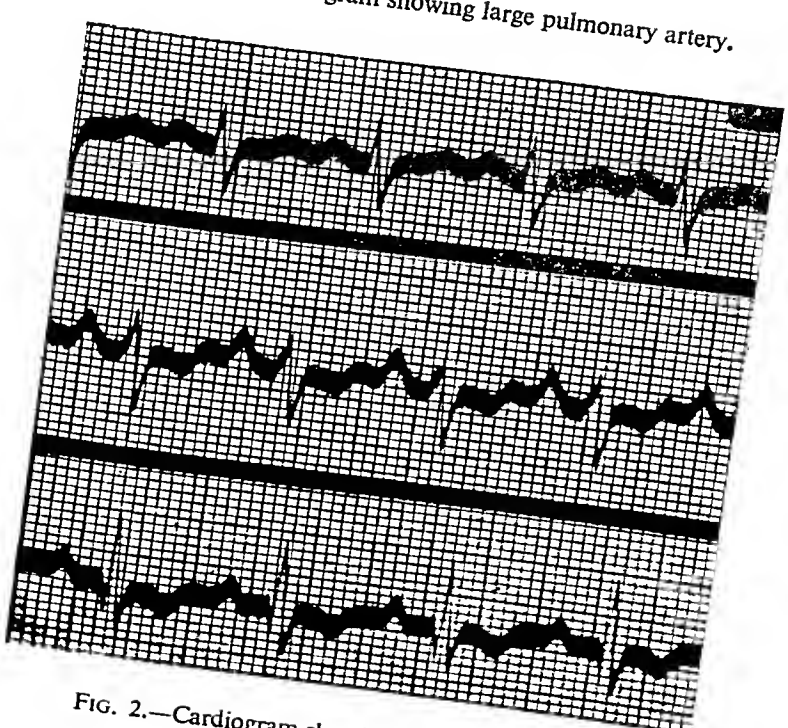

FIG. 2.—Cardiogram showing right axis deviation.

pericardium. Great dilatation of right side of heart, the cavity of both auricle and ventricle being about double the normal size. Considerable hypertrophy of right ventricle, its wall being stiff like a piece of leather. No hypertrophy or dilatation of left auricle or ventricle. Thickness of right ventricle 0·8 cm. Thickness of left ventricle 1·4 cm. The degree of hypertrophy was considerably more than is represented by these figures because of the great dilatation of the right ventricle. Brownish red, rather opaque myocardium; with frequent small greyish patches (0·1–0·2 cm. diameter) in the wall of left ventricle suggesting slight fibrosis; heart valves normal. Ante-mortem thrombus in right auricular appendage and also adhering to the wall of the right auricle at the site of the foramen ovale, which was patent (0·2 cm. diameter) but valvular. No clot projecting through the foramen into the left auricle nor any ante-mortem thrombus anywhere in the left side of the heart. Considerably enlarged hyperæmic and anthrocotic bronchial lymph glands, probably acutely inflamed, at hilum of left lung and at bifurcation of trachea. No abnormality of other lymph glands. Dilated stomach. Congestion and mucous catarrh of intestines. Chronic venous congestion of liver with œdematous connective tissue around the normal gall-bladder.

Small effusions of clear yellow fluid in each pleural cavity and in peritoneum (about 115 c.c. in each). Moderately enlarged firm " chronic heart failure " spleen. Congestion and cloudy swelling of kidneys. Two recent infarcts and an adenoma (0·4 cm. diameter) in left kidney. Bladder, prostate, and urethra normal, also testes and epididymis. Suprarenals, pancreas, thyroid, and pituitary normal; thymus for the most part replaced by fat. Normal brain. Middle ears clear. Pyorrhœa around bases of remaining teeth; teeth otherwise in fair condition; gums healed at sites of absent teeth. No clubbing of fingers; no œdema. Considerable cyanosis. Well-developed, well-nourished man.

Weight of Organs. Heart 455 g., left lung 610 g., right lung 710 g., liver 2080 g., spleen 280 g., right kidney 130 g., left kidney 155 g.

Microscopical Examinations

The Lungs. Six sections from different parts of the lungs show extensive disintegration of the alveolar walls, although only the anterior borders of the lungs are frankly emphysematous. In some areas—usually where alveoli are intact—capillaries are greatly engorged: elsewhere the tattered alveolar walls appear almost bloodless (Fig. 3). The contrast between the sharply defined patches of capillary engorgement and the surrounding zones in which it is difficult to distinguish any capillaries

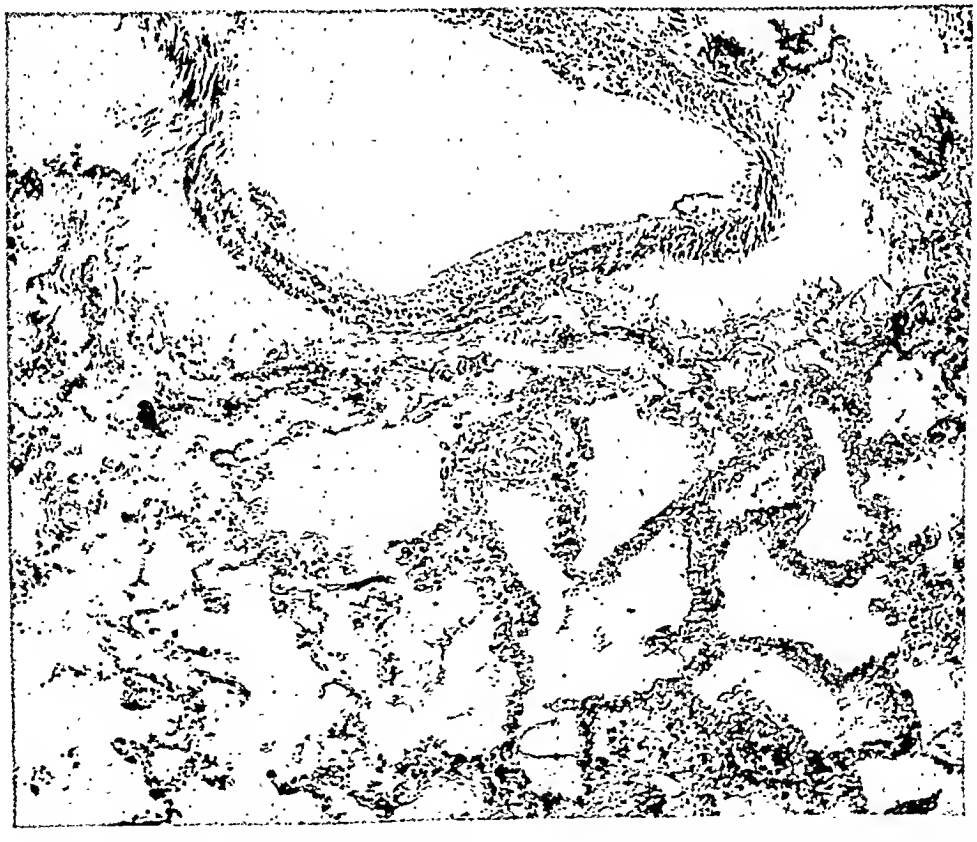

Fig. 3.—At the top, a small muscular artery with conspicuous intimal thickening; arteriole with greatly thickened wall in centre; area of capillary engorgement with preservation of alveolar pattern at bottom right; area of alveolar disintegration with few visible capillaries at bottom left.
Goldner's modification of Masson's stain. Magnification ×88.

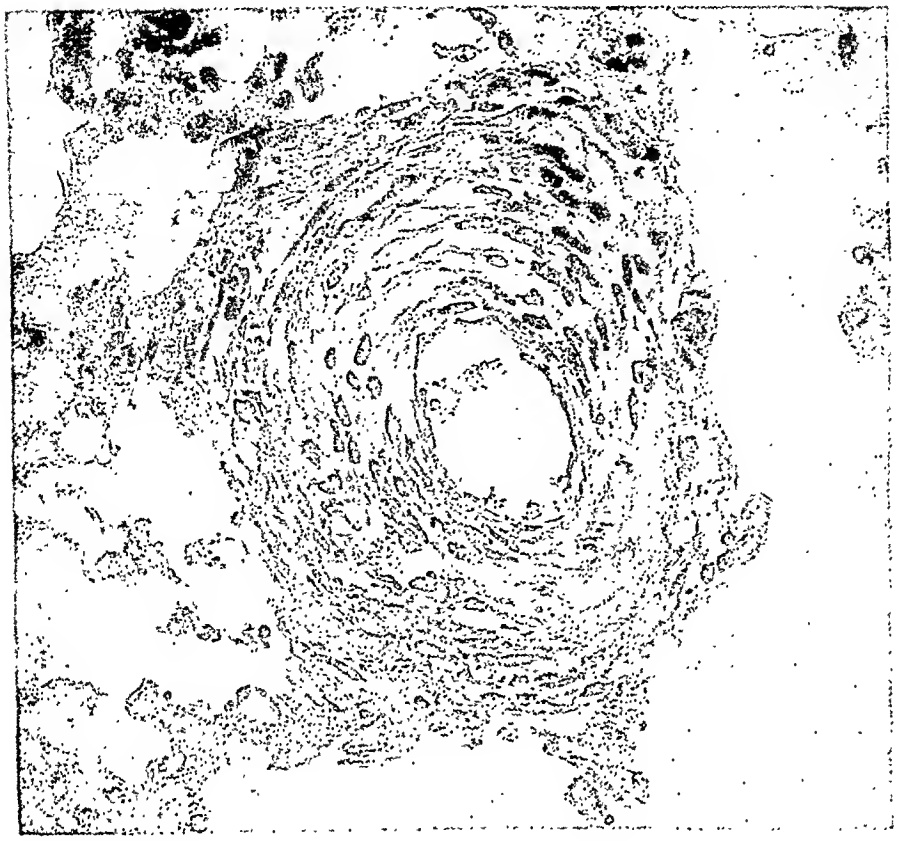

FIG. 4.—An arteriole more highly magnified, showing the characteristic lesion. Ehrlich's hæmatoxylin and eosin. Magnification ×390.

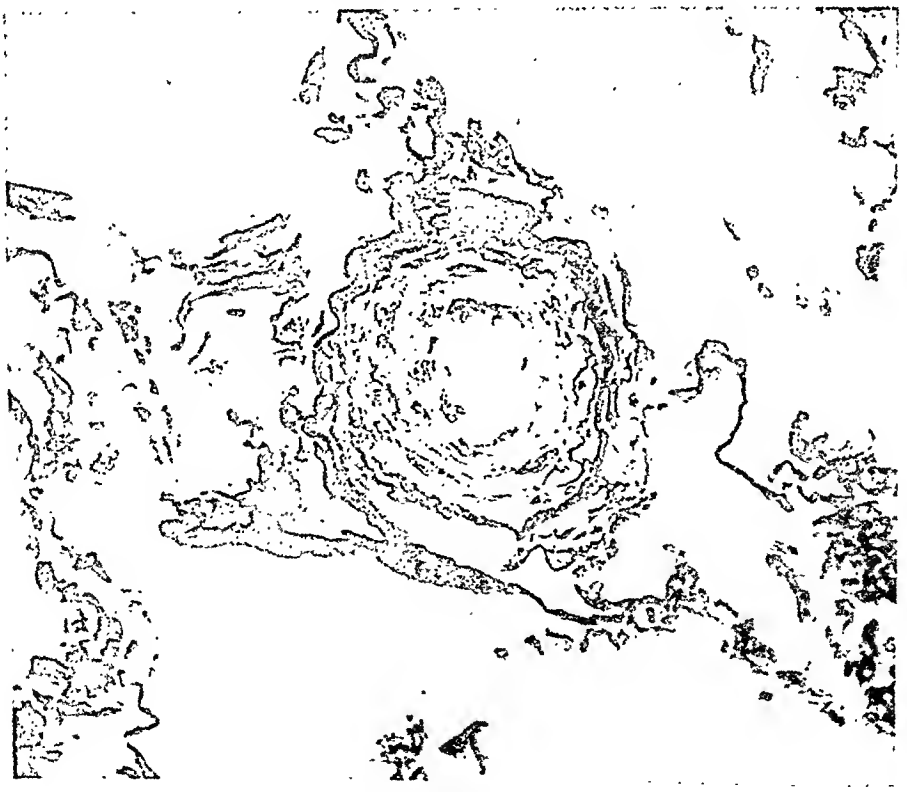

FIG. 5.—Another arteriole. The elastic fibril, which alone normally supports the endothelium, is seen as thick wavy black lines outside the concentric rings of cells.
Weigert's resorcin-fuchsin and neutral red. Magnification ×390.

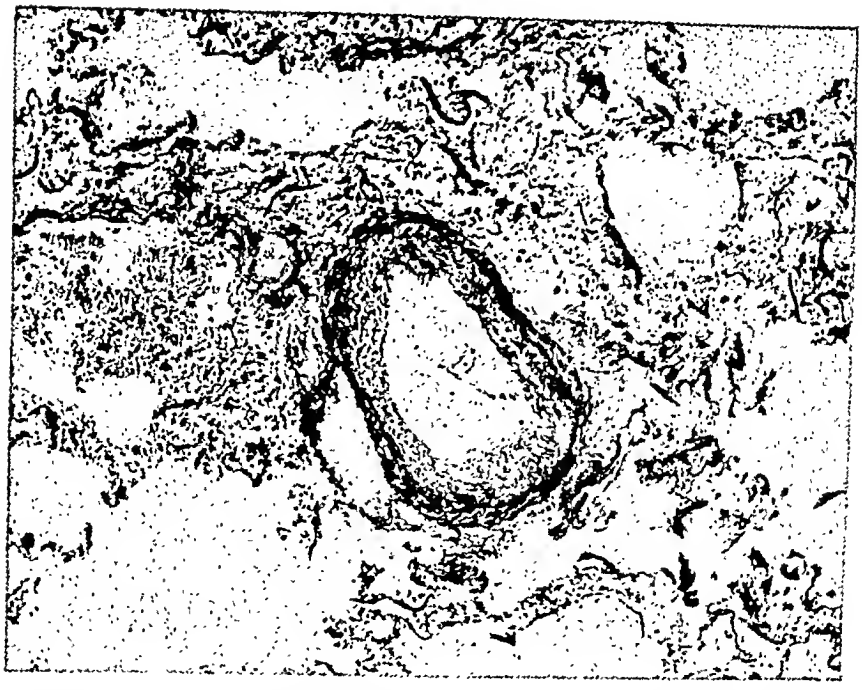

FIG. 6.—A small muscular artery. The internal and external elastic laminæ which bound the media are best seen on the left side. Weigert's resorcin-fuchsin and neutral red. Magnification ×88.

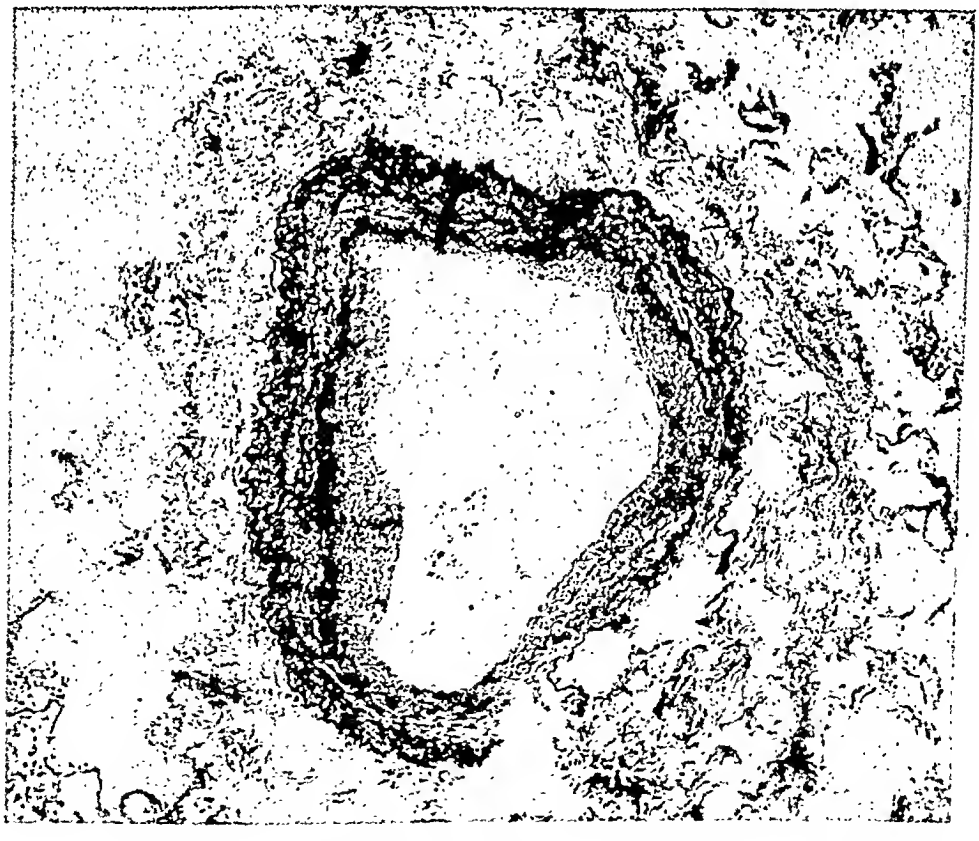

FIG. 7.—A pulmonary artery. Weigert's resorcin-fuchsin and neutral red. Magnification ×88.

at all, is very striking. Small hæmorrhages are present here and there, and many macrophages contain hæmosiderin.

Conspicuous abnormalities are present in pulmonary blood vessels of all sizes but are perhaps most notable in the arterioles and smaller muscular arteries. According to Brenner (1935) the wall of the pulmonary arterioles normally consists of endothelium supported only by a spiral strand of

elastic, but here in the affected arterioles the wall is greatly thickened and the lumen narrowed by the presence of a layer of spindle-shaped or elongated cells arranged concentrically between the endothelium and the elastic lamina (Fig. 4 and 5). The outlines of the individual cells are indistinct but in sections stained by Van Gieson's method the nuclei are set against a pale-pink background which sometimes contains a few deeper red collagen fibres. The cells are probably fibroblasts: in their appearance and staining reactions they are different from both endothelial cells and muscle fibres. Elastic fibres are not present amongst them. Sometimes their nuclei are not distributed evenly around the narrowed lumen but are arranged in two groups at opposite poles, as in the vessel shown in Fig. 6. The lesion is similar to the " hyperplastic arteriosclerosis " or " endarteritis fibrosa " of the arterioles of the kidney and other tissues in malignant hypertension; it is different from the true endarteritis obliterans of inflammation.

Great intimal thickening is also seen in many small muscular arteries in the lungs (Fig. 3 and 6). Here the thickened intima contains relatively fewer, more elongated and denser nuclei than in the arterioles, and fine elastic fibres and muscle fibres are present as well as collagen. There is no re-duplication of the internal elastic lamina. The media appears normal in structure but may be thickened, though the measurements that would be necessary to establish this have not been made.

In the larger pulmonary arteries (Fig. 7) both medial and intimal hypertrophy are conspicuous, and there is often much atheroma. The intimal thickening is sometimes of extreme degree.

The Heart and other Organs. In the heart, the fine fibrosis suspected macroscopically is not confirmed by histological examination but the muscle fibres of the left ventricle show rather wide separation. Chronic venous congestion and a subcapsular, probably adenomatous, nodule are present in the section of the liver; infarction and a cortical adenoma in the kidney. The blood vessels of all sizes in the heart, liver, and kidney are normal.

Discussion

Clinically the most striking features about this case were the steadily progressive symptoms and signs of right ventricular failure, unrelieved by rest in bed and full digitilization. Breathlessness on exertion was first noticed less than four months before death and there was not the slightest indication of lung or heart disease before this. During the last four weeks, although cyanosis and breathlessness on movement steadily increased, there was a notable absence of quickening of the pulse rate and respiratory rate at rest and there was practically no oedema.

In an analysis of 16 somewhat similar cases, Brenner (1935) states that the duration of symptoms varied from five months to five years, the average being less than two years, and that the course was steadily downhill, treatment being ineffective. In Navasquez' three cases (1940) the duration of symptoms in one was a year, in another two years and three months, and the third had been " chesty and bronchial " for a few years. In East's three cases (1940) it was two to three years in one, six years in another, and six months in the third. In Armstrong's (1940) it was four years. By comparison with these this case appears to represent an acute manifestation of the syndrome. It is possible that the stirring up of sepsis caused by dental extraction was an additional factor in precipitating failure.

On pathological grounds too there seems no doubt that this patient died of heart failure, and the hypertrophy and dilatation of the chambers of the right side of the heart together with the absence of any abnormality of the left side at once suggests increased resistance to the flow of blood through the lungs as the probable cause. The morbid changes in the lungs lend direct support to this view, for not only is there much disintegration of the alveolar walls with inevitable reduction of the capillary bed, but there is also widespread and severe disease of the pulmonary blood vessels. Both of these abnormalities would increase the resistance in the pulmonary circuit.

What is the relationship between the vascular lesions and the disintegration of the alveolar walls? The latter might cause vascular lesions by raising the pulmonary blood pressure, but on the other hand circulatory impairment due to vascular lesions might conceivably cause disintegration of the alveolar walls. It seemed to us that a comparison of the character of the vascular lesions with those known to be produced in the systemic circulation by hypertension might be helpful in deciding which were primary. As a result of such a comparison we are of the opinion that all of the vascular lesions are such as might reasonably be produced by hypertension alone, and that when compared with those seen in most patients who have died of emphysema or other disorders likely to have produced pulmonary hypertension they are of very unusual severity.

The occurrence of vascular changes of unusual severity in certain cases of systemic

hypertension is now generally recognized, such patients being said to be suffering from malignant hypertension. In a study of the structural changes in the lungs in mitral stenosis, Barker and Weiss (1936) have presented evidence of an analogous condition in the pulmonary circuit—"pulmonary hypertension with malignant sclerosis"—in which the arterioles in the lungs show hyperplastic arteriolosclerosis and, rarely, necrotising arteriolitis quite similar to the lesions seen in the systemic circulation in malignant hypertension. Though we have not found acute necrotic lesions in the blood vessels of the lungs of our patient, the resemblance of the arteriolar lesions to the hyperplastic arteriosclerosis has already been noted. It seems possible that both on clinical and pathological grounds this is a case of malignant pulmonary hypertension; that a rise of pulmonary blood pressure initiated the malignant sclerosis of the pulmonary arterioles which then exaggerated the pulmonary hypertension and set up a vicious circle. A vicious circle of this kind is probably the essential feature of malignant as distinct from benign hypertension and it explains the rapid worsening and early death of the patient.

If the vascular lesions were the result of pulmonary hypertension it is necessary to enquire how such hypertension arose. There is no satisfactory answer to this question. Undoubtedly the capillary bed was considerably reduced by disintegration of the alveolar walls, but it is impossible to do more than speculate as to whether this was sufficient to account for the hypertension and the origin of the alveolar disintegration remains a mystery. The most obvious explanation, that the patient was suffering from chronic emphysema, appears to us untenable. There was no clinical evidence of emphysema; no long history of cough or other chest trouble and none of the physical signs of emphysema, while post-mortem the existence of emphysema was not at first noticed, so slight was it. It cannot be denied that emphysema was present in the anterior borders of the lungs but this emphysema was atrophic in type, being merely part of the general disintegration of the lung, and there was no distension of the lung nor any formation of bullae. Thus the condition of the lungs was quite different from that seen in typical chronic emphysema. Furthermore Parkinson and Hoyle (1937) have shown that any gross degree of right ventricular enlargement is uncommon even in severe cases of chronic hypertrophic emphysema. In their series of 80 cases enlargement could only be demonstrated radiologically in 18 and in only 4 of these was it great. The case we are describing showed no clinical emphysema.

Summary

A patient is described who died of right ventricular failure within four months of the first appearance of symptoms. There was no previous history of heart, lung, or other disease. Progress was steadily downhill without any response to treatment.

Post-mortem, there was macroscopically conspicuous atheroma of the main pulmonary arteries and all its larger branches with great dilatation of the right side of the heart and hypertrophy of the right ventricle, the left side of the heart being normal. Emphysema was only visible along the anterior borders of the lungs and there was no distension of the lungs or formation of bullae.

Microscopically, there was conspicuous medial and intimal hypertrophy in the larger pulmonary arteries with much atheroma, and great intimal thickening in many of the small muscular arteries. Changes similar to hyperplastic arteriosclerosis of malignant hypertension were seen in the pulmonary arterioles. There was widespread disintegration of the alveolar walls without hypertrophic emphysema.

The significance of these changes is discussed.

We wish to thank Dr. Ff. Roberts for the X-ray examination, and Mr. H. P. Hudson for the photomicrographs.

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PRÆCORDIAL ELECTROCARDIOGRAMS

A COMPARISON OF CF AND V LEAD CONNECTIONS*

BY

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Received January 14, 1946

In the Michael Reese Heart Station, leads CF_2, CF_4, and CF_5 are used to record the præcordial electrocardiogram. This has been found to be satisfactory for ordinary clinical use (Katz, 1946). Other chest positions have been used and the chest electrode has been combined with different distant electrodes by others. Wilson and his school (Wilson *et al.*, 1944) have been recommending a special electrode to be combined with the chest electrode; this is the central terminal which connects the three limb electrodes (each through 5000 ohms resistance): the leads so obtained are called V leads. The theoretical advantages of these leads have been questioned (Katz, 1946, and Wolforth and Livesey, 1944). Præcordial electrocardiograms recorded by V leads and by CF leads obtained from chest positions 2, 4,

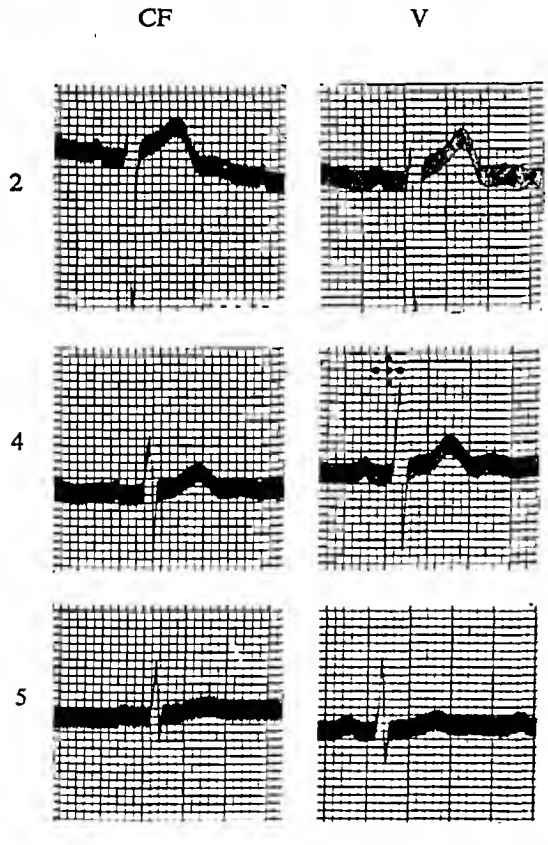

FIG. 1.—An example of CF and V leads in chest positions 2, 4 and 5, seen in about one-quarter of the normal subjects.

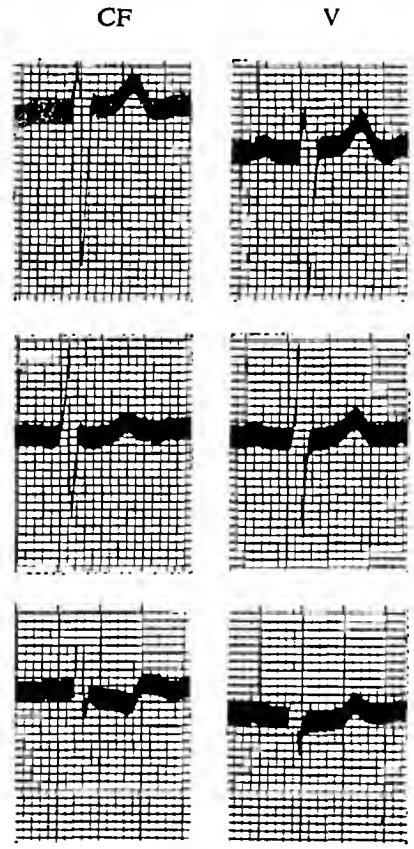

FIG. 2.—An example of CF and V leads seen in one-third of the cases with left heart strain.

* Aided by the A. D. Nast Fund for Cardiovascular Research. The department is supported in part by the Michael Reese Research Foundation.

and 5 were compared to determine how different they were from each other under various circumstances. This was done in order to determine whether or not the V leads offered any significant information of practical value not obtainable from the CF leads.

In order to make the records with V and CF comparable, they were taken immediately after one another for each of the three chest positions, the chest electrode being held in the same place while first the CF and then the V lead was taken. All records were standardized in the conventional manner, viz., 1 cm.=1 millivolt.. Ninety-one cases were investigated, the first sixty being taken at random and the last thirty-one being selected to fill out the various

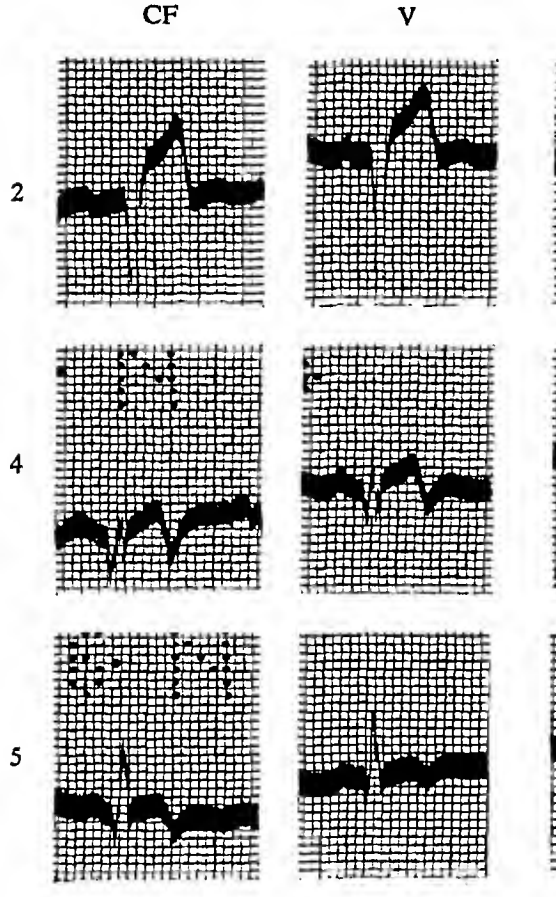

FIG. 3.—Comparison of CF and V leads in chest positions 2, 4 and 5 in subject with anterior wall infarction. Similar changes were found in about one-third of the cases.

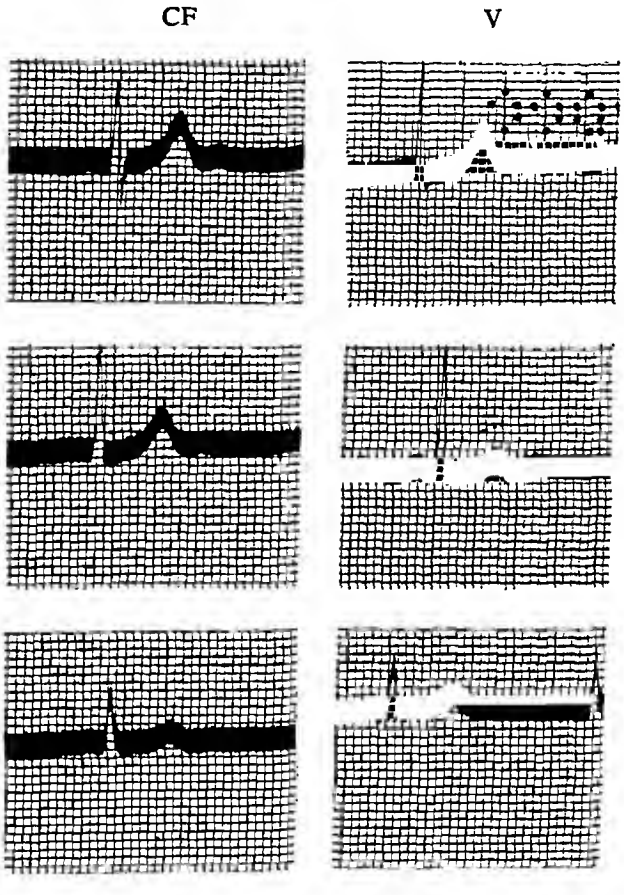

FIG. 4.—Comparison of CF and V leads in subject with posterior wall infarction. Similar changes were found in about half the cases.

groups in which we were interested. In several instances, more than one tracing was taken on the same individual. The cases included: (1) records that were within normal limits, some with right, others with left, and still others without either axis shift; (2) records with right, left, or combined heart strain patterns; (3) records with anterior wall, posterior wall, or atypical coronary patterns; (4) records with various types of intraventricular block; and (5) records with non-specific abnormalities. Three limb and the three CF and three V chest leads were taken in every case. The diagnostic criteria for classifying the records have been described elsewhere (Katz, 1946).

The CF and V records so obtained were analyzed for the comparative heights of the various deflections, viz., P, QRS, and T as well as the deviation of the S–T junction and S–T segment. The individual phases of QRS were also compared. The data are summarized in Table I and typical differences between CF and V leads for several of these groups are shown in Fig. 1 to 4. An instance showing an extreme difference is illustrated in Fig. 5.

The salient findings of this analysis may be summarized as follows.

1. The differences between the CF and V leads were numerically greatest in position 5, least in position 2, and intermediate in position 4. Thus, more differences were found as the chest electrode was moved to the left of the midline.

2. No significant changes in the QRS amplitude and contour, or in the level of S–T segment and S–T junction were noted. In general, T tended to be more positive in V leads than in CF leads in all types of curves and P tended to be upright more often in V leads than in CF leads.

3. There were no significant differences between V and CF leads in the group of cases showing (*a*) " non-specific abnormalities," (*b*) " right heart strain " patterns, (*c*) " combined heart strain " patterns, (*d*) " atypical coronary " patterns, and (*e*) the various types of " intraventricular block."

4. In about one-quarter (16 out of 57) of the leads from records that were " within

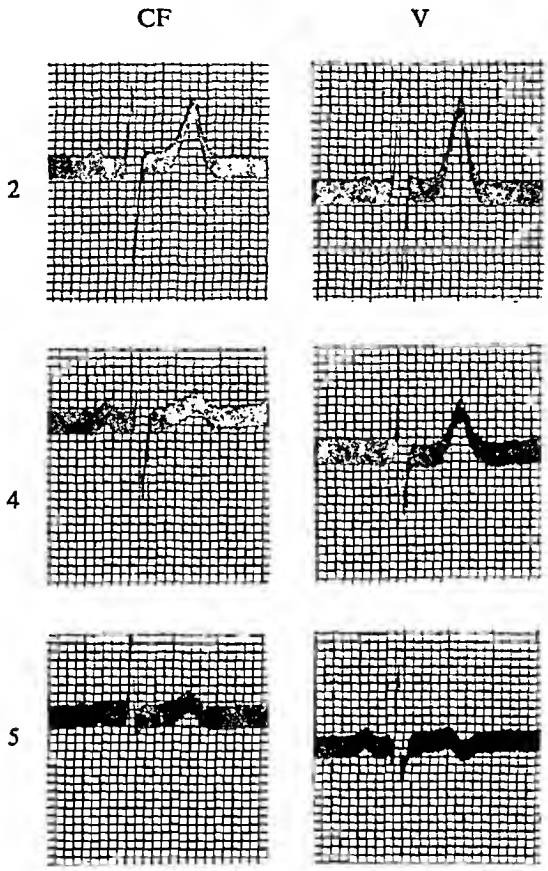

FIG. 5.—Comparison of CF and V leads showing unusual differences in subject with posterior wall infarction. These changes in position 5 occurred in one-third of the cases.

normal limits," T in V leads tended to be more upright (more positive) than T in CF leads; in the remainder, no differences were seen.

5. In the " left heart strain " pattern group there were minor to moderate differences in two-thirds (28 out of 45) of the leads. The trend was for the T waves to be more positive in V leads than in CF leads.

6. There were no differences in about one half (23 out of 45) of the leads between the T waves in V and CF leads in the " anterior wall infarction " pattern group. T was less inverted (more positive) in V than in CF in one third (15 out of 45) of the leads. Even in this group, the S–T junction and S–T segment deviations between V and CF leads were insignificant with but few exceptions.

7. In the " posterior wall infarction " pattern group, there were no differences between T in V and CF leads in about one-third (10 out of 27) of the leads. T was more negative in V than in CF in half (14 out of 27) of the leads. The tendency was for T to be less upright in V than in CF. In three instances T was inverted in V_5 while the corresponding T in CF_5 was upright.

TABLE I

DIFFERENCES BETWEEN V AND CF LEADS IN VARIOUS CONDITIONS IN 91 CASES

Chest Position	2	4	5
Records showing "Within Normal Limits": 19 Cases.			
No difference *	14	10	10
T_V more positive†	4	7	5
R_V taller	1	1	2
S_V smaller		1	3
S_V present			1
No R_V' S_V' present		1	
Records showing "non-specific Abnormalities": 10 Cases.			
No difference	6	3	1
T_V more positive	4	3	4
T_V more negative ‡		2	2
R_V taller	1		
S_V smaller		1	2
ST_V more negative			3
T_V less notched		1	
Records showing "Left Heart Strain": 14 Cases.			
No difference	7	4	3
T_V more positive	4	5	5
T_V more upright	4	3	2
T_V less inverted		2	3
T_V more negative	2		1
T_V less upright	2		
T_V more inverted			1
Q_V larger			1
Q_V smaller	2	2	1
R_V larger		1	
R_V smaller	2	1	
S_V larger	1	2	
ST_V less elevated	1	1	
ST_V more horizontal			1
Records showing "Combined Heart Strain": 3 Cases.			
No difference	2	2	2
T_V more negative	1	1	1
Records showing "Right Heart Strain": 4 Cases.			
No difference	2	2	2
T_V more positive	1	1	1
T_V more negative	1	1	1
Q_V larger	1		
R_V larger			1
ST_V more positive			1
ST_V more negative	1	1	1
S_V and S_V' smaller			1
Records showing "Intraventricular Block": 11 Cases.			
(1) Of the Common Type—4 Cases.			
No difference	2	2	3
T_V less inverted	1		
T_V more upright	1	2	1
QRS_V smaller	1		1
ST_V more elevated		1	
ST_V less depressed			1
(2) Of the S type—4 Cases.			
No difference	3	3	1
Q_V smaller	1		
T_V more upright		1	2
S_V deeper			1
(3) Of the Indeterminate type—2 Cases.			
No difference	1	1	1
T_V more upright	1		
T_V less inverted		1	
No R_V'	1	1	
R_V smaller			1
(4) Of the Uncommon type—1 Case.			
T_V less upright	1	1	
Records showing "Anterior Wall Infaretion": 15 Cases.			
No difference	10	9	4
T_V more positive	5	4	6
T_V more negative			1
Q_V present			1
R_V larger			1
S_V larger			2
S_V smaller			1
ST_V more elevated			1
ST_V less elevated	1	2	1
ST_V less depressed		1	
QRS_V larger		1	
Q_V smaller		1	1
Records showing "Posterior Wall Infaretion": 9 Cases.			
No difference	5	9	3
T_V more negative	4	6	6
T_V less upright	4	5	1
T_V inverted		1	
T_V more inverted			1
T_V inverted by TCF upright			3
T_V isoelectric			1
T_V more positive	1	1	
R_V smaller	2		
S_V larger		2	1
S_V smaller		2	
ST_V more positive			3
ST_V more negative		1	
QRS_V smaller		1	1
Q_VS_V small and present			1
Records showing "Atypical Infarction": 6 Cases.			
No difference		1	1
T_V more positive	4	3	3
T_V more negative	1	2	2
R_V taller		1	2
S_V larger		1	2
ST_V more negative	4	2	3
ST_V more elevated	1		
QRS_V small	1		

* Differences in amplitude of less than 5 per cent are considered insignificant.
† More positive means either less inverted or more upright. ‡ More negative means either more inverted or less upright.

CONCLUSION

Our experience reveals that the few differences encountered between these V and CF leads were minor. It would therefore appear that the V leads offer little if any diagnostic information not obtainable in the homologous CF lead. Since the supposed theoretical advantage has been seriously questioned, there appears no reason for those accustomed to the use of CF leads to substitute the V leads.

This study was suggested by Dr. L. N. Katz, and we are indebted to him and Dr. R. Langendorf for their advice in carrying out this study.

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BILHARZIAL HEART DISEASE IN EGYPT

COR PULMONALE DUE TO BILHARZIAL PULMONARY ENDARTERITIS

BY

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Received February 15, 1946

Of the various pathological causes of pulmonary endarteritis and right heart failure, schistosomiasis is probably the least familiar outside Egypt and other countries where the disease is endemic. It has long been known that bilharzia ova are sometimes deposited in the lungs (Belleli, 1885; Turner, 1909), and that adult worms of *S. hæmatobium*, often coupled males and females, may be found in the pulmonary vessels (Symmers, 1905; Day, 1937). In 1928, Sorour reported pulmonary bilharziasis as a common post-mortem finding in Egypt, and described small fibrous nodules due to ova deposited in the lungs, which he named bilharzial tubercles because of their semblance to the tubercles caused by Koch's bacillus. He also described a verminous lobular pneumonia due to the presence of dead bilharzial worms, and an "endobronchitis obliterans." Under the term "bilharzial atheroma," Sorour described deposits of ova in the intima of the pulmonary vessels resulting in endothelial proliferation, and he mentioned the wealth of new capillaries in the thickened intima, since recognized as a characteristic feature of bilharzial pulmonary endarteritis. In 1932 S. Azmy Pasha, of Cairo, recorded the first case of bilharzial heart disease observed clinically and pathologically. He described two cases with cardiac enlargement, gross dilatation of the pulmonary artery and pulmonary incompetence, associated with bilharzial hepatosplenomegaly. Necropsy was performed in one case and showed deposits of bilharzia ova in the lungs, obliterative endarteritis of the small pulmonary vessels, atheroma and dilatation of the main pulmonary trunks, and hypertrophy with dilatation of the right side of the heart; in addition, there were bilharzial lesions of the bladder and cirrhosis of the liver. Similar cases were later reported by Clark and Graef (1935) in a Porto Rican and by Day (1937) in Egypt. By far the most important contribution to the subject was made by Bernard Shaw and Ghareeb (1938) who described very fully the pathological changes of pulmonary schistosomiasis with special reference to the arterial lesions and to "Ayerza's disease."

Cor pulmonale with gross dilatation of the pulmonary artery is by no means a rare clinical finding in Egypt, certainly far more common than in England. It is usually encountered in young adults suffering from advanced visceral bilharziasis (Egyptian hepato-splenomegaly) or from severe genito-urinary infection with *S. hæmatobium*. Cor pulmonale occurred in 0·8 per cent of 520 consecutive cases of visceral bilharziasis admitted to the Kasr-el-Aini Hospital, and was found in 2·1 per cent of 282 consecutive autopsies on cases of schistosomiasis (Shaw and Ghareeb). The clinical diagnosis of "Bilharzial Ayerza's disease" is not infrequently made in the wards, and cases have been shown at clinical meetings (Mousa, 1942), yet the number of cases on record, in which both clinical and pathological findings are given, is scanty. The following new case is therefore reported.

CASE REPORT

A farmer, aged 34, was admitted to the Kasr-el-Aini Hospital under Dr. Gaafar. For three years he had suffered from dyspnœa on exertion, cough with slight expectoration, and præcordial pain. For several years he had noticed hæmaturia at the end of micturition.

On examination he was breathless at rest, but not obviously cyanosed. There was no clubbing of the fingers. The neck veins were not engorged and there was no œdema. The rhythm was regular; the blood pressure, 120/80 mm. The apex was in the fifth interspace, four inches from the mid-line. There was visible and palpable pulsation in the first and second left interspaces, with dullness on percussion to the left of the sternum in this area. Auscultation showed an accentuated first sound and soft systolic murmur at the apex, and a much accentuated pulmonary second sound. The chest was emphysematous in shape, but there were no added sounds over the lungs. The liver and spleen were enlarged and firm.

X-ray of the chest (Fig. 1) showed an aneurysmal swelling in the region of the main

FIG. 1.—Radiograph showing aneurysmal dilatation of pulmonary artery and its right branch in the hilum. The aortic knob is invisible.

pulmonary trunk without any visible aortic knob, and the right pulmonary artery in the hilum formed a swelling of aneurysmal proportions. The heart was enlarged to right and left. There was no obvious fibrosis of the lungs. Urine contained a trace of albumin, red cells, pus cells, and living ova of bilharzia hæmatobium. The stools contained ankylostoma ova. Wassermann reaction, negative: blood-count; red cells 4,660,000; white cells 7800 (polymorphs 62 per cent, lymphocytes 26 per cent, eosinophils 10 per cent, monocytes 2 per cent).

Three weeks after admission he became suddenly worse. He complained of pain over the liver, the cervical veins became engorged, marked cyanosis appeared, and gallop rhythm was audible at the apex. The liver became more swollen, jaundice developed, and he died a few days later.

NECROPSY

Heart weight, 550 g. (approx.). The pulmonary trunk was grossly dilated, forming a sac 6·5 cm. in diameter; the circumference just above the valves was 13·5 cm. Both main branches of the pulmonary artery formed aneurysmal swellings which were almost circular, and 7 cm. in diameter. On opening up the artery, the main trunk showed thickening of its wall and intimal atheromatous plaques. The walls of both main branches were thickened and the seat of advanced ulcerated atheroma; their lumina were filled and almost occluded

by ante-mortem thrombus of some standing. Atheroma extended into the medium-sized arterial branches in the lungs (see Fig. 2 and 3).

The aorta was hypoplastic, with a circumference above the valves of 6 cm., and showed slight intimal atheroma but no evidence of syphilitic aortitis. The heart itself showed gross enlargement of the right side, both ventricle and auricle being dilated to about three times their normal capacity. The right ventricle was much hypertrophied, its wall being 1·3 cm.

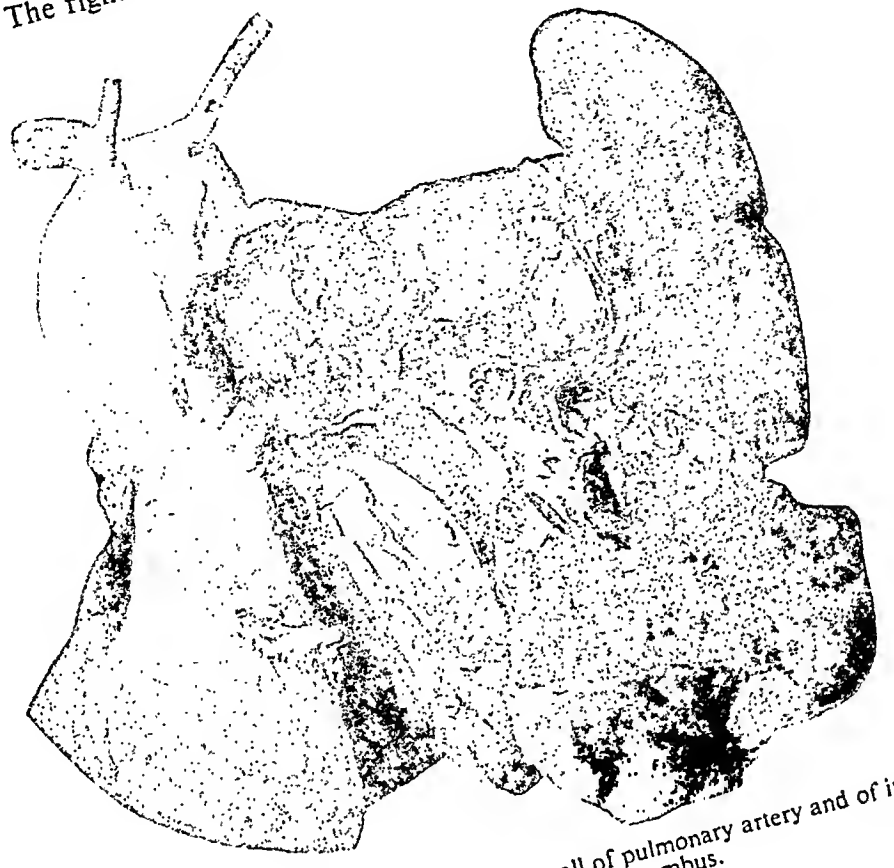

FIG. 2.—Heart and attached left lung with anterior wall of pulmonary artery and of its left branch removed to show contained thrombus.

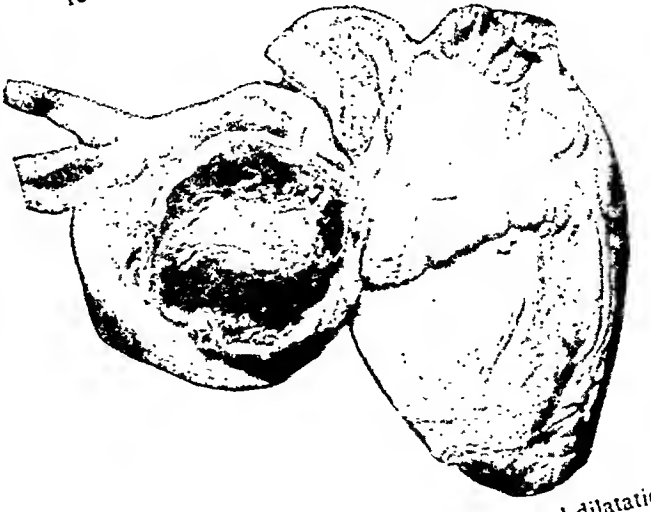

FIG. 3.—Heart and aorta viewed from right, showing aneurysmal dilatation of right pulmonary artery and occluding thrombus.

thick, and the auricle was also hypertrophied. The left ventricle was normal. All the valves were healthy, and both inter-auricular and ventricular septa were intact.

The lungs were congested but free from bilharzial tubercles. The liver weighed 1400 g.; it was coarsely granular and congested, and the naked eye appearance was suggestive of bilharzial cirrhosis. The spleen weighed 750 g.; its capsule was thickened and its pulp fibrotic. The intestines appeared normal. The bladder showed a "sandy patch" at the trigone, and ova of *S. hæmatobium* were present in scrapings. The ureters were normal and the kidneys showed congestion only.

Histology

Lungs. Sections from both lungs were examined. The alveoli were normal except for some degree of venous congestion and extravasation of red cells. The pulmonary arterioles were much thickened and showed marked obliterative endarteritis (Fig. 4). There were numerous "angeiomatoids," both of capillary and cavernous type, typical of bilharzial pulmonary arteritis (Fig. 5). Bilharzia ova were seen in relation to some of the arterioles;

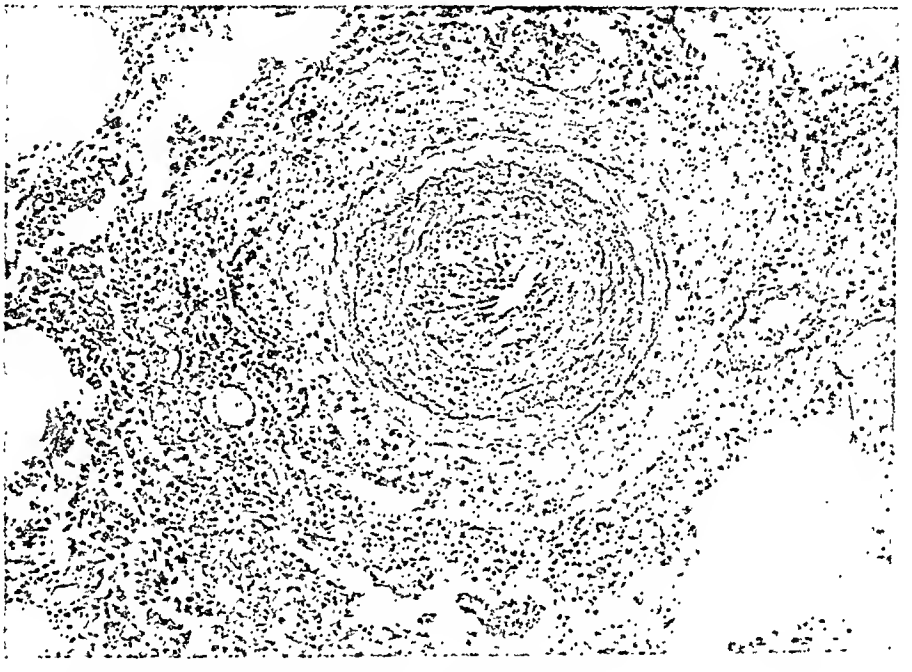

Fig. 4.—Section showing small pulmonary vessel occluded by canalized intimal thickening.

the ova were distorted and shrivelled and sometimes occupied by giant cells (Fig. 6 and 7). In the interstitial tissues, ova were scanty and calcified. Sections stained by Levaditi's method did not show any spirochætes.

Pulmonary arteries. Sections from the trunk and two main branches showed atheroma with calcification. The adventitia showed thickened vasa vasorum with perivascular infiltration by lymphocytes and plasma cells. There were minute foci of cellular infiltration in the media, but no destruction of the musculo-elastic coat suggestive of syphilis, and no spirochætes could be found in sections stained by Levaditi's method. In the main branches, there was organized thrombus of moderate age.

Aorta was normal, except for some cellular infiltration of the adventitia, and there was no evidence of a syphilitic lesion.

Liver showed periportal cirrhosis of the type usually produced by bilharzial disease in Egypt.

Spleen showed hyalinosis of the central arterioles of the lymphoid bodies. Sinusoids were filled with red cells and histiocytes. The trabeculæ were prominent and there were fibro-siderotic nodules which gave the prussian blue reaction. Bilharzial pigment both intra-

and extra-cellular was present, but no parasites or ova were seen. The histological picture was that usual in endemic splenomegaly.

Bladder and colon showed deposits of calcified ova in the submucosa.

Anatomical diagnosis. Pulmonary endarteritis due to bilharziasis; atheroma and aneurysmal dilatation of the pulmonary artery and main branches, with thrombotic occlusion. Hypertrophy and dilatation of the right heart. Cirrhosis of liver; bilharzial splenomegaly; bilharzial cystitis.

Discussion

Pathology. Adult worms may be found in the lungs where, when dead, they produce a focal verminous pneumonia, and later become calcified. The more important pulmonary lesions are, however, caused by the ova which reach the lungs as emboli from the normal habitat of the worms and become impacted in the pulmonary arterioles. In the case of *S. hæmatobium*, the ova travel direct from the systemic veins to the right heart and lungs. In the case of *S. Mansoni*, which inhabits the portal tract, ova must reach the systemic veins via collateral venous channels which develop when the liver has become cirrhotic.

Shaw and Ghareeb classify pulmonary bilharzial lesions as follows:

(1) Parenchymatous tubercles.

(2) Focal arterial lesions.

(3) Widespread arterial lesions causing " Ayerza's disease."

Ova of both *S. hæmatobium* and *S. Mansoni* infest the lungs, but the latter more often cause arterial lesions. The ova become impacted in the arterioles causing a necrotizing arteriolitis, and may then pass through the vessel wall, destroying the media, and so become extravascular, when they form bilharzial tubercles. Healing of the vascular lesion causes

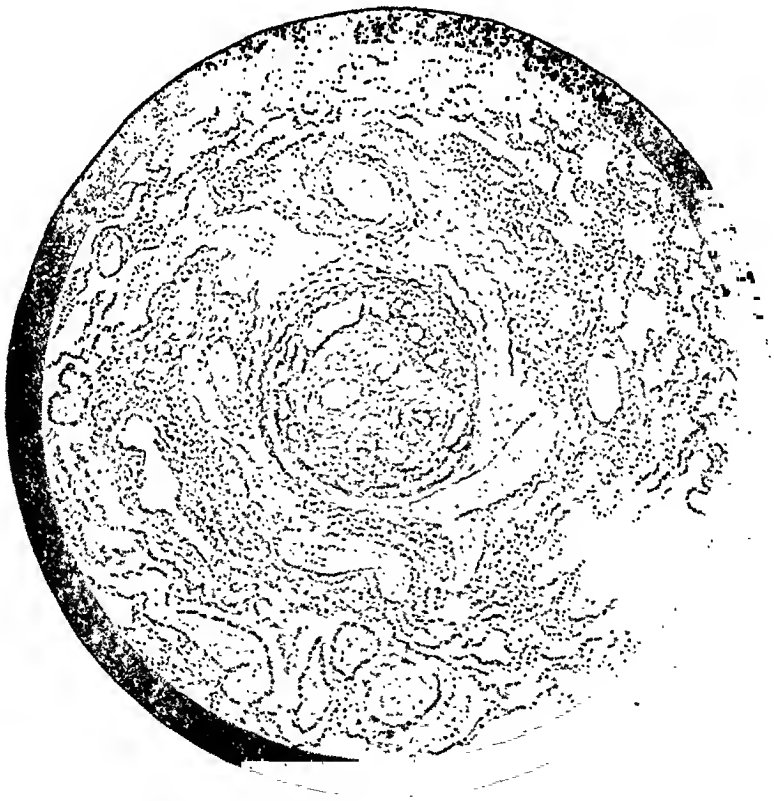

Fig. 5.—Drawing of section showing angeiomatoid formation round occluded and vascularized pulmonary vessel.

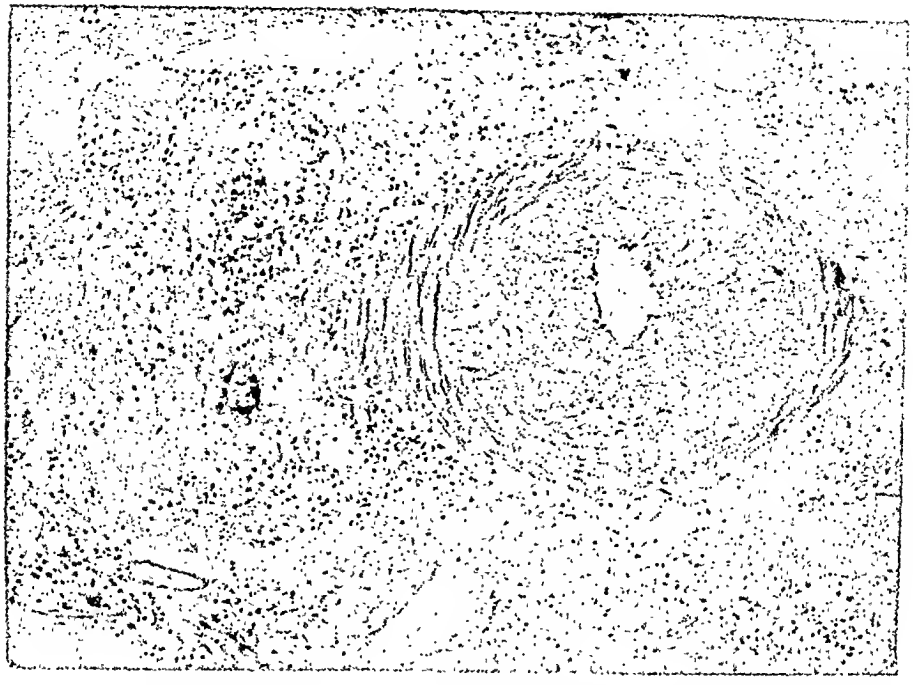

FIG 6.—Section of thickened pulmonary vessel with adjacent giant cell filling shell of ovum.

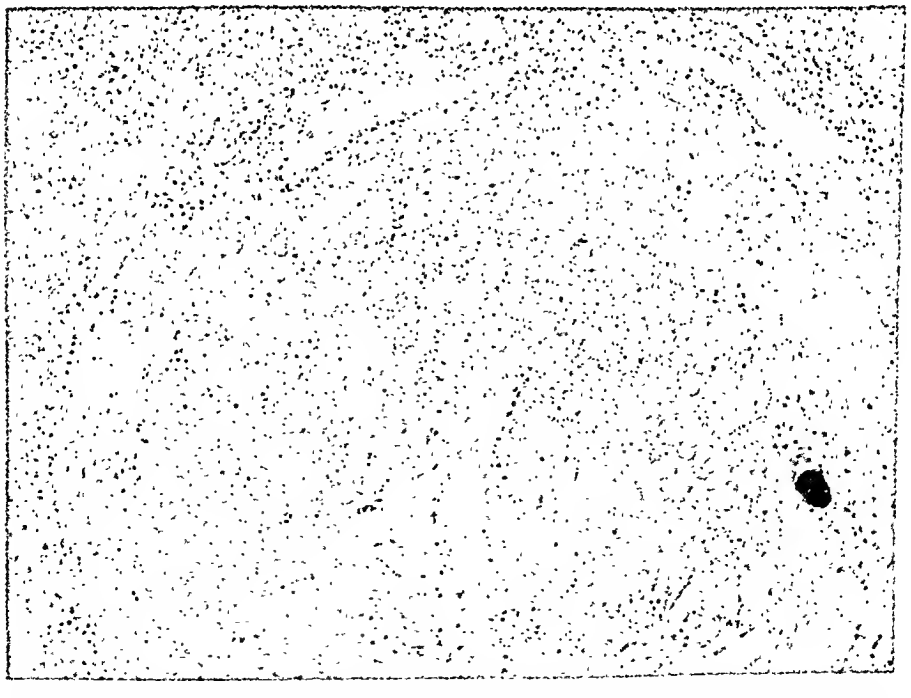

FIG. 7.—*Section showing obliterative endarteritis of pulmonary arteriole, the wall of which contains a calcified bilharzia ovum and adjacent angeiomatoid formation.*

obliterative endarteritis. Shaw and Ghareeb have shown that the distinctive histological feature of bilharzial arteritis in the lungs is the formation of " angeiomatoids." The occluded vessel becomes canalized by new capillaries, some of which dilate forming blood spaces lined by endothelium and, in the absence of an intact medial coat, this vascularized tissue expands beyond the normal confines of the vessel and may reach cavernous dimensions. They found no evidence that angeiomatoid formation was the result of thrombosis followed by canalization of the arterioles, for when this happens the vascular tissue is contained within an intact media. Clark and Graef (1935) also described highly vascularized tissue expanding the vessels in bilharzial arteritis of the lungs, and they too excluded canalized thrombosis as the explanation; they also noted extravascular granulomas containing endothelial lined channels. Serial sections are necessary in order to demonstrate the relation of the angeiomatoids to the vessel lumen.

In the earlier stages of bilharzial infection of the lung, ova may be seen in the vessel walls (Fig. 8) and in extravascular tubercles, but later, when there is widespread obliterative arteriolitis, and enlargement of the right heart, the ova may be scanty or absent, and angeiomatoids

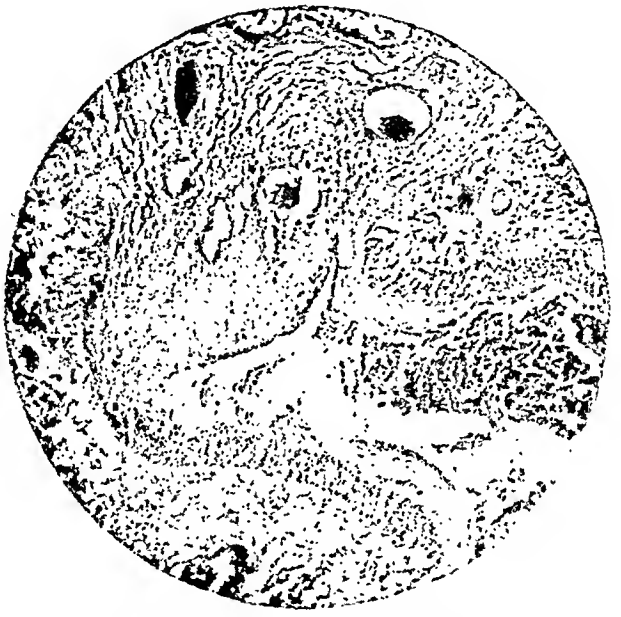

FIG. 8.—Section showing bilharzia ova embedded in intima of small pulmonary vessel. (*By the courtesy of Prof. Sorour.*)

may then be the only evidence of a bilharzial ætiology. Shaw and Ghareeb believe that massive and repeated embolism of the lungs by ova is necessary to cause pulmonary hypertension and enlargement of the right ventricle.

Vessels proximal to the obstruction show medial hypertrophy and intimal thickening which is a reaction to pulmonary hypertension, and the larger branches show atheroma. Occlusion of the main pulmonary arterial branches in the hila by organized thrombus, as occurred in the present case, has also been reported in aneurysmal dilatation of the pulmonary arterial tree due to atrial septal defect (Bedford, Papp, and Parkinson, 1941); it occurred in three of Brenner's cases of primary pulmonary arteriosclerosis, and in others cited by him (Brenner, 1935). In Azmy's case of bilharzial pulmonary arteritis, one main branch was occluded by clot regarded as embolic.

While changes in the pulmonary vessels are undoubtedly the cause of the cardiac enlargement and failure in bilharziasis, the myocardium is, occasionally, directly involved, and Clark and Graef found scanty ova of *S. Mansoni* surrounded by miliary foci of fibrosis, in both ventricles. In the case of *S. Japonicum*, Strong (1944) cites a case reported from Japan in which numerous bilharzial tubercles with giant cells occurred in the ventricular myocardium, so that sections viewed by low power resembled tuberculosis.

Clinical features. In Egypt, bilharzial cor pulmonale usually occurs in young adults aged 20 to 35 years, but proven cases as young as 12 and 13 years have been recorded (Shaw and Ghareeb). The condition is encountered mainly in residents of the Nile Delta, where infection with *S. Mansoni* is endemic and where hepato-splenomegaly is prevalent. Compared with other forms of chronic cor pulmonale, the bilharzial variety affects younger subjects and does not usually cause much cyanosis or clubbing of the fingers. The absence of cyanosis has been attributed to an associated anæmia due to hookworm infestation, but even in the absence of anæmia cyanosis is seldom severe, except as a terminal event. A more probable explanation is the fact that, in bilharzialis, the pulmonary lesion may be almost confined to the arterioles, leaving the alveolar and capillary structure intact (Mousa, 1942). In fact, bilharzial lung infection may amount to a primary pulmonary arteritis, and its main effect is to cause pulmonary hypertension and hypertrophy of the right heart. In the more common varieties of cor pulmonale, the vascular lesion is associated with chronic disease of the lung parenchyma, and it is the latter that interferes with oxygenation of the blood in the lungs and thus causes cyanosis. Radiographs of the chest in bilharzial heart disease rarely show any significant changes in the lung fields apart from vascular dilatation, and evidence of fibrosis is usually lacking.

Brenner (1935), in discussing primary pulmonary vascular sclerosis states that cyanosis is usually intense, but he cites cases, including syphilitic ones, in which it was absent. In theory, provided the lesion is limited to the arterioles and the hypertrophied right ventricle can maintain an adequate flow against the increased resistance, there is no reason why cyanosis should occur; it would be expected only when the right ventricle fails. Indeed, the classical clinical picture of so-called Ayerza's disease is really one of chronic lung disease and heart failure combined.

Mainzer (1938) has described the X-ray appearance of miliary infiltration of the lung fields in pulmonary bilharziasis, but at the Kasr-el-Aini Hospital these miliary shadows in the lung fields have only been observed during the course of antimony treatment, and are regarded as due to an allergic reaction around the ova. Clinically, some degree of emphysema, with or without bronchitic signs, is the usual finding in the chest.

The radiological appearance of the heart may be indistinguishable from that of atrial septal defect. Not only is the pulmonary trunk grossly dilated, but the hilar branches may also reach aneurysmal size, a feature regarded as especially characteristic of atrial septal defect. Pulmonary incompetence from enlargement of the valvular orifice is common in both conditions.

The main diagnostic problem is, therefore, to differentiate between bilharzial and congenital heart disease. The presence of bilharzial lesions elsewhere is, of course, important. All recorded cases of bilharzial heart disease and all cases that we have observed have also had hepato-splenomegaly, and some have also had lesions of the urinary tract. The presence of ova in the stools and urine should always be sought. The blood may show an eosinophilia, but less frequently and to a lesser degree than in the earlier stages of bilharzial infection. The intradermal reaction of Fairley may be positive even when ova are no longer to be found in the stools or urine.

SUMMARY

A case of chronic cor pulmonale with aneurysmal dilatation of the pulmonary artery, due to bilharzial endarteritis of the pulmonary arterioles, is described, and the pathological and histological findings are given.

The clinical and pathological features of the disease as it occurs in Egypt are briefly reviewed. It affects young adults, aged 20 to 35 years or even younger, infected with *S. Mansoni* or *S. hæmatobium* or both, and suffering from Egyptian hepato-splenomegaly.

Cyanosis and clubbing of the fingers are slight compared with that seen in other forms of chronic pulmonary heart disease, and clinical and radiological signs of lung disease are slight or absent. Dilatation of the pulmonary artery may amount to aneurysm, and relative pulmonary incompetence is common. The X-ray appearance of the heart is similar to that of atrial septal defect.

Pathologically, the changes are mainly vascular, and consist of an obliterative endarteritis of the pulmonary arterioles, atheroma and dilatation of the main vessel, and hypertrophy and dilatation of the right ventricle. Histologically, bilharzia ova may be identified in the walls of the small vessels and in extravascular tubercles. In the later stages, the occluded vessels become expanded by highly vascularized tissue to form "angeiomatoids," which are a distinctive feature of bilharzial arteritis.

We wish to thank Dr. M. Gaafar for permission to record the above case, and Prof. M. F. Sorour for his help with the pathological investigation and for the microphotographs in Fig. 4–8. One of us (D. E. B.) is much indebted to many Egyptian colleagues for the opportunity of seeing cases and for information about the clinical features of bilharzial heart disease.

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MECHANISM OF THE WOLFF-PARKINSON-WHITE SYNDROME

BY

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Received January 23, 1946

The Wolff-Parkinson-White syndrome has been described frequently during the past few years, and there is considerable evidence now that the short P–R interval associated with an aberrant QRS is probably due to short circuiting of an auricular stimulus through one or more accessory bundles.

Hunter, Papp, and Parkinson (1940) came to the conclusion that the syndrome represented a double rhythm by two interfering pacemakers, one near the sinus and the other in one bundle branch, but Wolferth and Wood (1941) raised objection to this hypothesis, and adhered to their previous theory (1933) put forward to explain this type of cardiogram, namely, that the ventricular asynchronism is due to premature stimulation of one ventricle by conduction through the bundle of Kent. Parkinson and others described gradual changes of P coinciding with gradual changes in the ventricular complex, and argued against the bundle of Kent hypothesis. Wolferth and Wood, however, thought there was as much variation between the P waves before aberrant as there was before normal complexes, and quoted a case of Tung (1936) in which the P waves became smaller and the QRS complexes normal twenty minutes after the injection of atropine; thirty minutes after the injection the P waves had returned to their normal size, while the QRS complexes still remained normal. It was suggested that the atropine may be a factor in this change in the character of the P wave. Butterworth and Poindexter (1944) suggested that fusion beats may be the explanation of the cardiographic changes in this syndrome. Rosenbaum, Hecht, Wilson, and Johnston (1945) used unipolar leads from the œsophagus, præcordium, and other parts of the thorax, and gave observations supporting the presence of one or more accessory conducting bundles. Stein (1945) described a case showing normal P–R intervals and complexes alternating with those of the Wolff-Parkinson-White syndrome immediately after cessation of attack of paroxysmal tachycardia, suggesting also a shorter accessory pathway between the auricles and ventricles. Öhnell (1944) in a comprehensive monograph " Pre-excitation—a cardiac abnormality " showed various types of this syndrome. He assumed that there were two excitatory waves, the regular impulse via the bundle of His and an additional premature ventricular spread. These sometimes varied in time in the same case, and he described this as a " concertina effect."

The following (Case 1) showed all the features of this Wolff-Parkinson-White syndrome. A boy, aged 17, was admitted to the Aberdeen Royal Infirmary on June 12, 1942, complaining of palpitation which was found to be due to paroxysmal tachycardia. He had three attacks of palpitation during the previous year, and, except for one fainting attack, after a strenuous game of football, there were no other symptoms. He gave no history of any serious illness. On physical and X-ray examination there was no abnormality of the cardiovascular system. Cardiograms were obtained showing paroxysmal tachycardia (Fig. 1), and others showing the characteristic *Sh. P–R : B.B.Bl.* syndrome—a short P–R interval and the QRS of the bundle branch type (Fig. 2). Since his discharge from the hospital in August 1942 he has had paroxysms of tachycardia, occurring at varying intervals and lasting from a few minutes to several hours. During these he had palpitation and breathlessness, but at other times he felt quite fit.

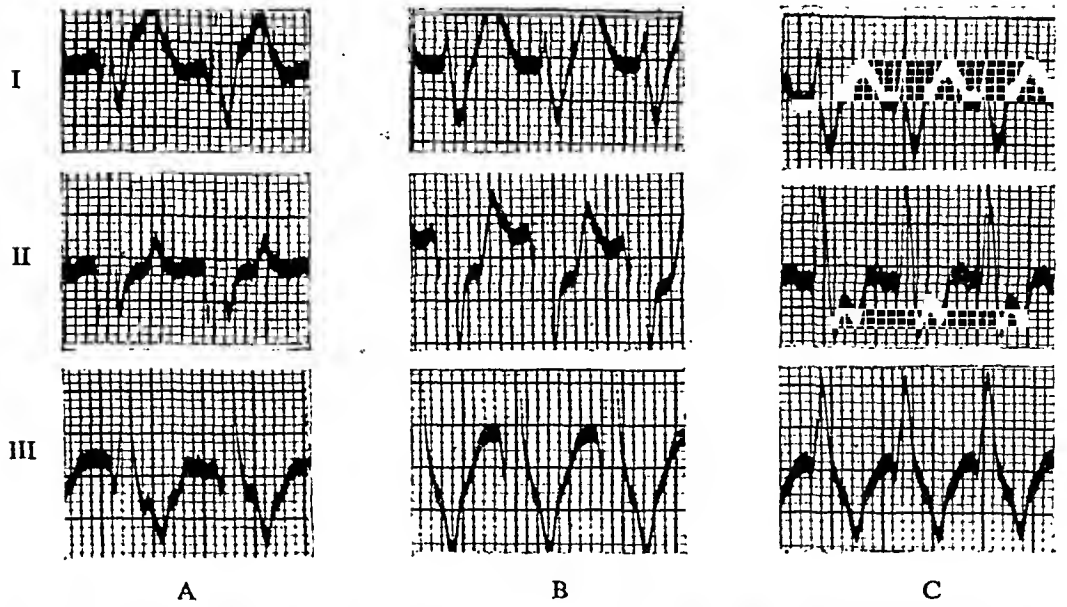

FIG. 1.—Case 1. Paroxysmal tachycardia. (A) 15/6/42. (B) 27/8/42. (C) 30 minutes after atropine.

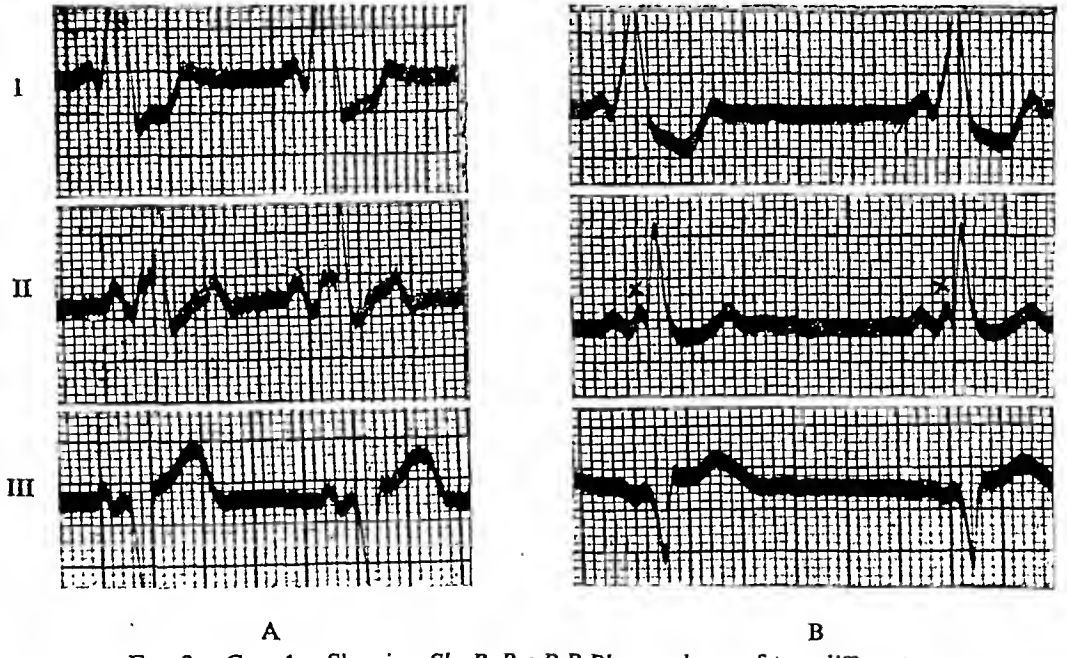

FIG. 2.—Case 1. Showing *Sh. P–R : B.B.Bl.* complexes of two different types.

CARDIOGRAPHIC ANALYSIS

The cardiograms in Fig. 2 and 3A show, especially in leads I and III, the typical short P–R interval and the widened QRS complex, somewhat resembling a left bundle branch block. Fig. 1 shows paroxysmal tachycardia, and other figures illustrate the effect of 1/50 of a grain of atropine given subcutaneously.

The following features are worthy of note.

(1) When the *Sh. P–R : B.B.Bl.* rhythm is present, the complexes are not all similar (Fig. 2 and 3A): there is a variation of P waves, of QRS complexes, and of S–T segments. This indicates variability in the path followed by the impulse over both auricles and ventricles. Öhnell (1944) would regard the differences in the complexes as due to a variation in the interval between the beginning of two assumed ventricular excitation waves.

(2) The second leads in Fig. 2B, Fig. 3A, and Fig. 5B and D show, after each P wave, another upward deflection (afterwards indicated as X) just before the QRS complex.

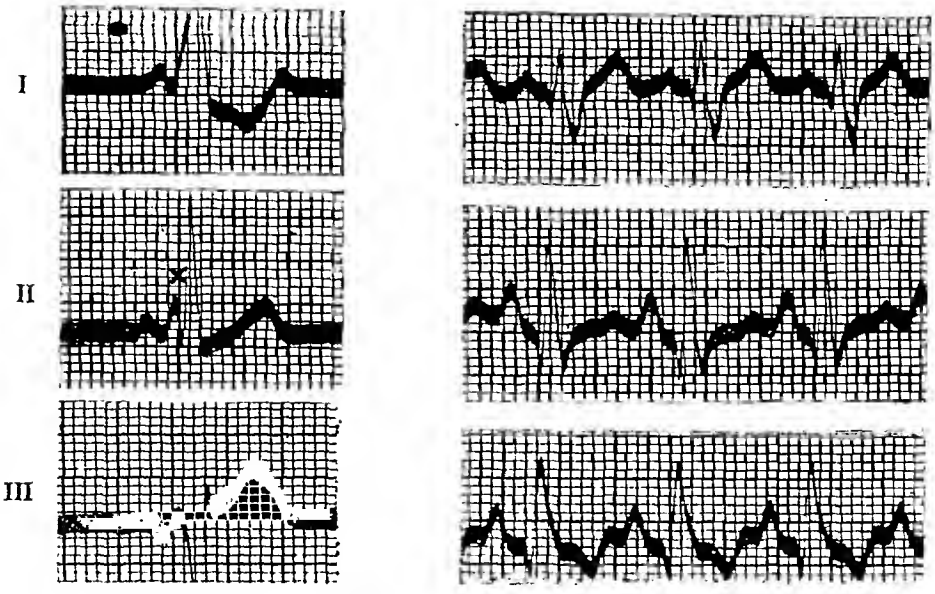

FIG. 3.—Case 1. 2/9/42. (A) *Sh. P–R : B.B.Bl.* complexes immediately before injection of 1/50 grain atropine. (B) 15 minutes after injection of atropine.

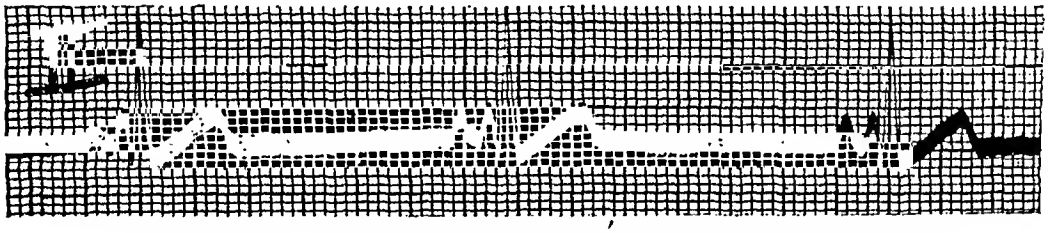

FIG. 4.—Case 1. 2/9/42. After atropine showing variation of P waves.

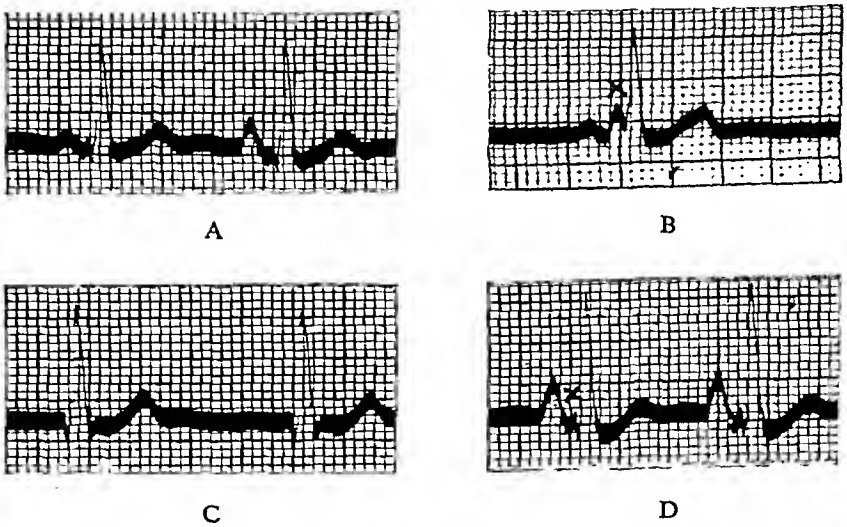

FIG. 5.—Case 1. 2/9/42. After atropine. All lead II. (A) Showing further variation of P waves. (B) Note relative size of P and X waves. (C) Showing change of pacemaker to A-V node. (D) Compare with Fig. (B). Change in size of P and X waves.

(3) The length of the P–Q interval in lead II of Fig. 3A, where the abnormal rhythm is present and the interval includes an X deflection, is equal to that of the P–Q interval in lead II of Fig. 3B. This shows right bundle branch block after atropine, but the P–R and the P–Q intervals may be considered normal. It may be noted that the configuration of QRS is similar to that in the paroxysmal tachycardia in Fig. 1.

(4) Atropine can modify the P waves and QRS complexes in many ways.

(*a*) Fig. 4, and 5A, B, and D, show P waves of varying sizes and shapes, mostly followed by X waves, which also vary.

(*b*) The P–R intervals in Fig. 5A are shorter than the assumed normal interval in Fig. 3B.

(*c*) Fig. 5C shows nodal rhythm with disappearance of P and X.

Discussion

The cardiograms suggest two special comments. The variation in shape of the P waves and the P–R intervals points to changes in the position of the pacemaker. There is room for considerable variation of its position within the sheath of muscle described anew by Glomset and Glomset (1940). Abnormal lability in its position seems to be one feature of the disorder.

Secondly, the shape of the ventricular complex in most cases of the syndrome shows two peculiarities. The first is a thickening and slurring of the initial rise of R with resultant widening of the complex; the second is an abnormality of the S–T segment tending to make the whole complex diphasic but less so than in ordinary bundle branch block. It would appear, therefore, that the excitatory stimulus to the ventricle is abnormal and also premature. This may be explained by assuming an accessory bundle joining the auricles and ventricles. If an excitatory wave from the auricles passes down the main A-V bundle, it cannot stimulate the part of the ventricular muscle that is already responding to the accessory bundle stimulation. Whether the greater or earlier stimulus to the ventricle is through the main bundle or through an accessory bundle probably depends on the position, size, and conducting capacity of the accessory junctional tissue. Assume accessory junctional tissues either on the right or left side of the main bundle (A C or B C in Fig. 6). Suppose the auricular stimulus reaches the A-V node (AV), and another point A, the beginning of the accessory junctional tissue, at the same time; if A–C is shorter or of higher conductivity than AV–C, C may be stimulated through A before the excitatory impulse from A-V arrives. There will, therefore, be a change in the cardiogram during the P–Q interval depending on the distance

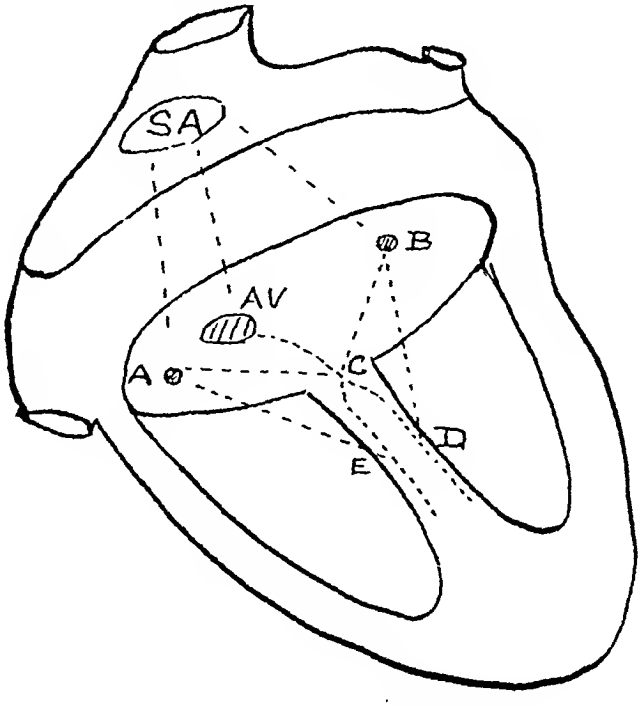

Fig. 6.—Diagram of the heart. See text.

of A and AV from C, and the rates of conduction of A–C, AV–C. The accessory junctional tissues may possibly be longer, A–E or B–D, and there would be short circuit stimulation in the region of one of the main branches, either right or left, depending on the position of the accessory conducting tissue.

The main A-V bundle is normally well insulated from the surrounding muscular tissue and the stimulus is conducted to the branches before there is response of the ventricular muscle. An accessory bundle may not be so completely insulated, resulting in infiltration of the stimulus to the ventricular muscle during the passage from A to C or A to E, and partly explaining the variation of the beginning of the QRS complex.

An accessory bundle (or bundles) between the auricles and ventricles may be the commonest cause of this early excitation of the ventricles, and in support of this theory are the post-mortem results of Öhnell (1944) and Wood, Wolferth, and Geckeler (1943), but there are other possible causes. Anatomical abnormalities occur in all tissues and an accessory branch from the bundle proximal to the main division should be kept in mind as a possible cause of pre-excitation.

In these cases of accessory junctional tissue, the auricular impulse therefore finds the shortest and easiest way to the ventricle and when the sympathetic and vagal mechanisms are stabilized, the auricular stimulation apparently pre-excites the ventricle, but if the vago-sympathetic control is changed by atropine or other drugs, the conduction capacity of junctional tissues is changed. Wilson (1915*a*) showed that even normal rhythm could be converted into auriculo-ventricular with right bundle branch block by stimulation of the vagi, and that by administration of atropine normal rhythm could be restored. He concluded that the vagi were partially responsible both for the change in the location of the pacemaker and for the abnormality of the ventricular complexes. Wilson (1915*b*) also found it possible to produce A-V rhythm in a large proportion of young persons by vagus stimulation during the intermediate period between injection of atropine and the appearance of its maximum effect, and he inferred a selective action of atropine on the vagal endings in the A-V node. The same author (1915*c*) described cases showing changes in the location of the pacemaker associated with respiration. The changes were of three kinds—migration of the pacemaker within the intermediate neighbourhood of the pacemaker, migration to the A-V node, and complete auriculo-ventricular dissociation. In the *Sh. P–R : B.B.Bl.* syndrome there is no doubt that in the majority of cases, including the first case presented above, atropine has this action on the pacemaker. Öhnell (1944) has described various ways of changing the mechanism in these cases—by carotid sinus pressure, by holding the breath, and by change of posture. Quinidine medication has also been shown to change the excitatory mechanism, possibly by its effect on the conducting tissues.

It seems, therefore, that the auricular stimulus in the Wolff-Parkinson-White syndrome is transmitted to the ventricles by the main bundle and an accessory bundle. By decreasing the vagal control, the stimuli through the main bundle are increased, and those through the accessory bundle decreased. This may be due to a relatively increased conduction capacity of the main bundle or due to a change of the position of the original pacemaker nearer the A-V node, favouring increased excitation through the main bundle.

As indicated in Fig. 6 an accessory bundle may be long (A–E) causing premature stimulation of the ventricle some distance from the main bundle and short-circuiting in the region of a branch. This type may show a cardiogram of the typical *Sh. P–R : B.B.Bl.* syndrome, but the accessory tissue may be less extensive (A–C, Fig. 6) and the premature excitation may be only very slight. Another case is given to illustrate this.

A medical man (Case 2), aged 35 years, who was being treated for pulmonary tuberculosis by artificial pneumothorax, had a severe attack of paroxysmal tachycardia in 1945. He gave the history of having similar attacks when he was a student. When he was seen soon after the paroxysm in 1945 there was nothing abnormal found on physical examination in the cardiovascular system, but a cardiogram (2/11/44) (Fig. 7) showed a small wave (X) between P and Q. On 8/11/44 (Fig. 8) the X wave was absent, but there was slurring at base of QRS. The history of attacks of paroxysmal tachycardia and the abnormality in cardiogram suggested pre-excitation of the ventricles. After atropine the slurring of QRS disappeared (Fig. 9). A cardiogram taken on 9/5/34 (Fig. 10) showed a similar abnormality at the base of QRS,

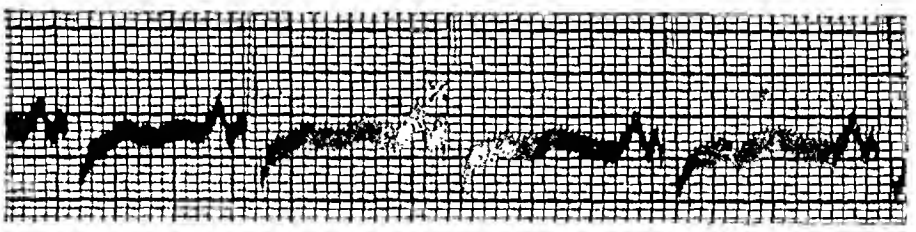

FIG. 7.—Case 2. 2/11/44. After an attack of paroxysmal tachycardia showing small X wave after P.

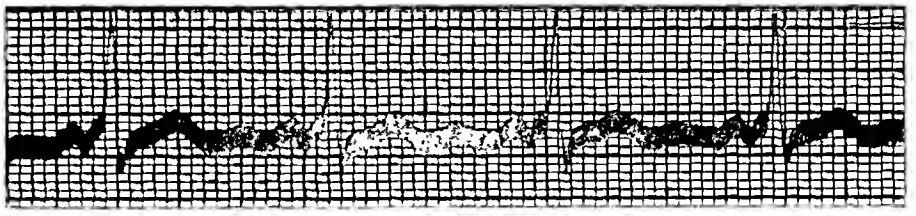

FIG. 8.—Case 2. 8/11/44. Showing slurring at base of QRS.

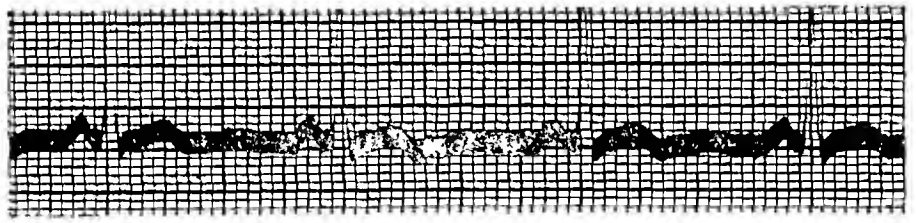

FIG. 9.—Case 2. 8/11/44. Showing disappearance of slurring after atropine 1/50 grain.

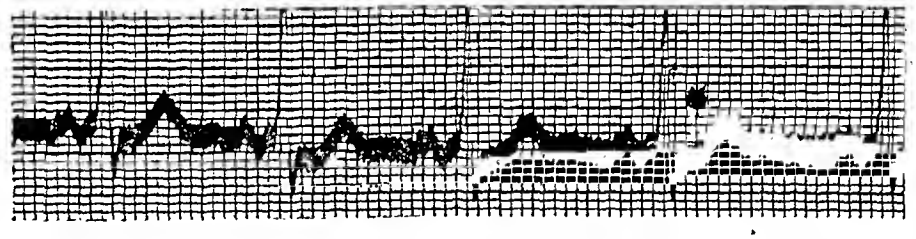

FIG. 10.—Case 2. 9/5/34. Cardiogram taken ten years previously showing abnormality at base of QRS.

showing that this pre-excitation had been present for at least ten years. This case would appear to have a minimal change in the cardiac conducting tissues (as compared with the more marked changes in the first case showing the typical *Sh. P–R : B.B.Bl.* syndrome). Pre-excitation may, therefore, vary in degree.

Doubtful cases showing slurring at the base of QR, especially if there is a history of attacks of paroxysmal tachycardia, should be investigated by means of atropine or by one of the other methods mentioned by Öhnell.

Disease or injury of the main junctional tissues may be a cause of pre-excitation of the ventricles. Accessory bundles could be present without pre-excitation showing, provided the conduction capacity of these is relatively small as compared to that of the main bundle. But if the latter is affected by disease, such as diphtheria, the auricular stimulus will tend to take the next easiest path—the accessory tissue which may be present but normally inactive. Pre-excitation of the ventricles will then result. Cookson (1945) describes a case of diphtheria showing what is almost certainly ventricular pre-excitation. If there had been no accessory junctional tissue, probably complete heart block would have occurred.

There may be little or no change in the cardiogram after the administration of atropine, suggesting that conduction through accessory tissue is more permanent or fixed and not influenced by changes in the vago-sympathetic mechanism. This is illustrated in another patient.

A girl (Case 3) aged 21, a munition worker in Coventry, was seen in the out-patient department of the Aberdeen Royal Infirmary on 6/10/44. She gave a history of attacks suggesting paroxysmal tachycardia and the cardiogram (Fig. 11A) showed a short P–R interval and broadening of the QRS complex, almost certainly due to pre-excitation of the ventricle. The maximum change after atropine is slight (Fig. 11B).

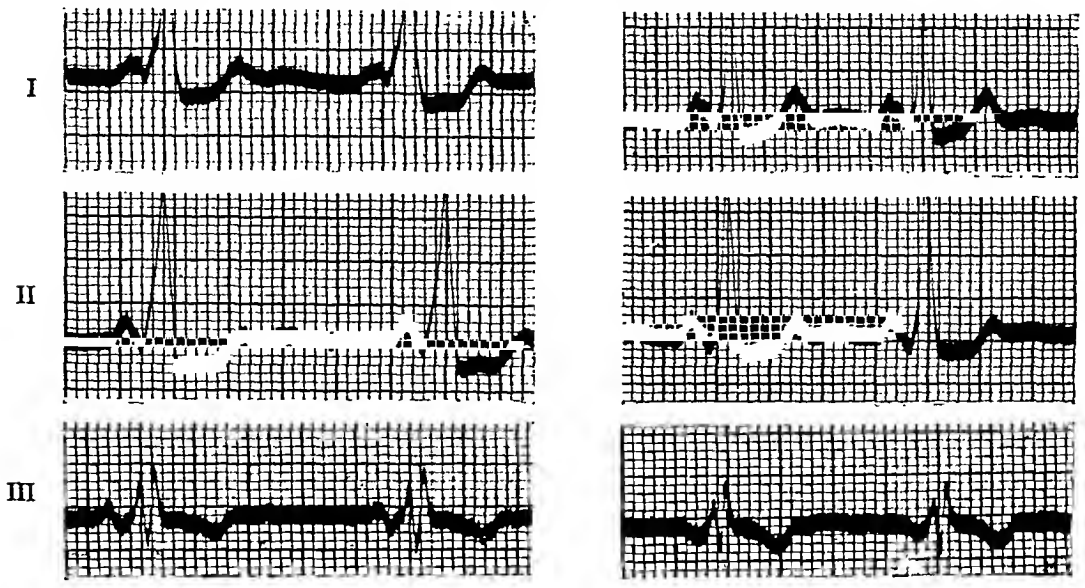

FIG. 11.—Case 3. (A) Cardiogram of girl with a history of attacks of paroxysmal tachycardia showing *Sh. P–R : B.B.Bl.* complexes. (B) Cardiogram showing only slight changes after atropine 1/50 grain.

SUMMARY

A typical case of the Wolff-Parkinson-White syndrome is described and the mechanism discussed. Premature excitation (or pre-excitation) of the ventricle is probably the cause, and published autopsy reports suggest that this is due to accessory conducting bundles between the auricles and ventricles. Other abnormalities, such as an accessory branch of the main bundle, could cause pre-excitation and should be looked for in future autopsies.

Pre-excitation may vary in degree. The degree of short-circuiting of the auriculo-ventricular conduction may depend on the position of the accessory bundle or bundles and generally changes or disappears with variation of the vagal tone.

A case has been described showing slight pre-excitation which has been present for at least ten years.

Pre-excitation is generally demonstrated by changes in the P–Q interval after injection of atropine, but a case with almost fixed pre-excitation is described.

I wish to express my thanks to Dr. W. F. Croll and to Professor R. S. Aitken for valuable help in preparing this paper. I am indebted to Dr. John Parkinson for literature and helpful criticism of an unpublished paper, and to Dr. A. Rae Gilchrist for the cardiogram of Fig. 10.

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POSTURAL HYPOTENSION

BY

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Received March 21, 1946

Postural, or better, orthostatic, hypotension was first described in 1925 by Bradbury and Eggleston. The outstanding symptom, a profound fall in blood pressure on standing up, is one of a triad. The other two, less dramatic, but none the less important and almost constantly present, are anhydrosis and impotence.

The disease is almost entirely confined to males, and only two out of twenty-four reported cases have been women. The age at which symptoms are first noted has been anything from 28 to 70 years.

Accounts of the first appearance of symptoms are not always full, but it is clear that in a fair proportion the first indication of the onset of the disease is anhydrosis; this has sometimes been there for a number of years before the symptoms of hypotension have attracted attention. Impotence appears to come later; usually with or after the hypotension.

Report of a Case

The following is an account of the investigation of a case which presented characteristic features.

J. M. was an engineer, aged 57, married, with four children. He had a severe attack of typhoid at 45; at 49 he suffered from metal poisoning: his occupation at that time led him to handle brass, gun metal, and phosphor-bronze, and sometimes he put a valve of this material in his mouth. Up to the age of 55 he still played tennis. He had felt the cold of recent years.

Syncopal attacks. At the age of 50 he began to suffer from what he called fainting attacks, which came on when he was standing up, never when sitting or lying. Before the attack he used to feel giddy and unsteady; his legs trembled and his hands began to shake, and he could no longer stand up; and he had to drop straight down and sit crouched or leaning forward holding his head down, semi-conscious. Sometimes he lost consciousness. The attack lasted several minutes; after a little he would recover and could go on walking. During the last few years the attacks had become more frequent. Apart from the giddiness, the attacks were not particularly unpleasant; there was no nausea, nor sinking feeling in the abdomen, nor sweating. Usually the attacks were more frequent in the morning than in the afternoon.

Anhydrosis. He had never sweated on his face and for the last four years has not sweated at all. For many years he only sweated on the left side of his body. This had been noted by his fellow workers, for only one side of his shirt became damp.

Impotence. About the age of 37 he became impotent and has had no sexual activity or desire since. He was never constipated.

This account is fairly characteristic of this disorder, and the observations on the blood pressure given below confirm the diagnosis.

Physical examination. A small thin man, rather bent, looking rather younger than his years. Height, 5 feet 2 inches, weight 8 stone 4 pounds. His demeanour was alert and active. His skin was inelastic and dry, with a greyish pallor. The growth and distribution of hair

was normal. His voice was high-pitched and rather piping. The testes were not atrophied. There was nothing abnormal in the heart or arteries: the skiagram of the chest was normal and so was the cardiogram. All other organs, including the central nervous system, appeared to be healthy. The Wassermann reaction was negative.

The Effect on the Blood Pressure of Changes in Posture

These observations were made with the patient lying on an electrically operated tipping-table. When tilted from horizontal to 35° head upwards in 7 seconds, the blood pressure would fall about 40 mm. systolic and 25 mm. diastolic in a minute. The heart rate remained unchanged. The results were much the same when the patient was tilted to 90° head upwards. After being upright for two minutes the systolic pressure was 50 mm., and the diastolic unreadable.

It was thus possible to study the effect of raising the angle of the body to the horizontal without movement. It was found that the main fall in pressure occurred in the first half-minute. The systolic and diastolic pressures fell about equally, though diastolic readings were hard to obtain; the rate of the heart remained unchanged. There was not much further fall in pressure when the patient was raised to 90°, instead of 45°. These passive alterations in posture caused the blood pressure to fall in much the same way and to about the same degree each time. The results were typical of numerous observations.

On tilting the patient head downwards, the pressures rose from 110/75 to 145/90 at 35° head downwards, and to 170/90 at 45°. The rate of the heart did not change. On returning the patient to the horizontal the pressures resumed their original level.

Similar results to these have been noted by many observers. There is no really satisfactory explanation for them. The blood distributes itself in the body under the influence of gravity as though the arterial bed were unprovided with a vaso-constricting mechanism. Further, this lack of adjustment in the arterial bed can be shown by raising one limb.

Effect of raising the arm. With the patient recumbent the pressure was 110/80: when the left arm was raised vertically the brachial pressure fell to 88/54. With an initial higher pressure the fall was the same. Raising the other arm did not affect the blood pressure in the horizontal arm. The fall in pressure, averaging 25 mm., is about equal to the amount of the difference in hydrostatic pressure in the raised arm and the pressure at the level of the heart.

A similar effect was noted when the arm was raised vertically when he was sitting up.

Recumbent, B.P. 85/50. Sitting up, B.P. 70/50

Pressure in arm raised to level of brain, B.P. 45/?

In Sanders' case (1931) similar readings were obtained, although in other respects this patient differed considerably, as is noted elsewhere.

Effect of postural hypotension on the secretion of urine. The tendency to low levels of blood pressure during the day affects the efficiency of the kidneys, and nocturia may be a very troublesome symptom for these patients. For the past six years this man used to pass urine five or six times at night and rarely during the day. The output of urine was recorded over a series of seven consecutive days, the night time being reckoned from 9 p.m. to 9 a.m., the patient being up during the day, and the fluid intake being left to his inclination. The output during the day varied from 10 to 22 oz.; during the night from 28 to 50 oz. Bradbury and Eggleston (1925) made similar observations.

When resting in bed the blood urea was 67 mg. per 100 c.c. The urea clearance was 53 per cent of the average maximum normal. After being up for nine hours, the blood urea was 77 mg. per 100 c.c., and the urea clearance fell to 32 per cent of the average standard normal.

In a somewhat atypical case of postural hypotension reported by Corcoran, Browning, and Page (1942) the injection of angiotonin increased the blood flow through the kidneys and the renal excretion. This is the opposite to what is usually found, as the effect is vaso-constriction in normal persons. Presumably the general vaso-constriction improved the renal flow, and outweighed any local constriction of the renal arterioles.

Effect of reducing venous return to the heart. The patient was asked to blow up a column of mercury to 30 mm., and keep it there as long as possible (Flack test). With the patient

recumbent the B.P. was 112/75 and the pulse 80. On starting the test the B.P. fell at once to 50/35 and there stayed until the end of the test. After a minute it then rose to 105/60. The pulse rate remained unchanged throughout. Woofter and Deibert (1943) have made similar observations.

The effect of this test is to raise the intrathoracic pressure and reduce the cardiac intake. It would appear that the patient was unable to adjust his arterial system to meet the diminished output. In the normal person this test causes no fall in blood pressure.

When this test was carried out with the patient inclined head downwards, MacLean and Allen (1940) noted that it could be done quite well. The reason for this must be that there is adequate venous return, or that the arterial system is well filled already. The latter is more likely: for when the test is performed by the patient standing, Laufer (1942) found that the fall in blood pressure was more severe than when sitting, or lying, when it was least. It is unlikely that diminished venous return is the sole cause of postural hypotension, as MacLean and Allen (1940) suppose, in view of other evidence.

Other Observations

Sweating. Pilocarpine (1/10 grain) was given hypodermically. Seven minutes later both axillæ were moist, and a minute later both sides of the chest were sweating, likewise the face. As pilocarpine stimulates the sweat glands or the post-ganglionic endings of their sympathetic nerve supply, the response to the drug shows that these structures are intact.

On the other hand, when the patient was put in a hot-air bath for fifteen minutes, he did not sweat. Immersion in water as hot as he could bear caused no sweating on the face. This observation suggests that the anhydrosis is due to a central lesion.

Blood counts. When he first came under observation there was some anæmia—red blood corpuscles, 3·2 million, Hb. 68 per cent, C.I. 1·07. Several blood transfusions were given, and three months later the count was 3·9 million, Hb. 75 per cent. The resting gastric juice contained no acid ; after histamine injection there was free HCl. equivalent to 42 c.c. N/10. A moderate degree of anæmia has rarely been noted in this disease.

Peripheral vasomotor reflexes. In order to get some idea of the site of the lesion in this disease, various peripheral vasomotor reflexes have been investigated. A defective carotid-sinus reflex has been thought to be a cause. Vasomotor reflexes depending on stimulation with heat and cold, and the effects of emotional and painful stimuli, have given varying results.

Carotid sinus reflex. Persons vary a good deal in their reaction to pressure on the carotid sinus. In this patient there was very slight slowing and little or no fall in pressure. Other observers have found that the rate may fall along with the pressure in the usual way (Ellis and Haynes, 1936): on the whole the fall in pressure is more notable than the slowing. Stimulation of the sinus with cyanide has produced hyperpnœa (Ellis and Haynes, 1936). It has been suggested that failure of the carotid sinus to react might lead to postural hypotension; but these results show that it is not always incapable of reacting to stimuli, and would exclude it as a cause.

Reaction to cold and other peripheral stimuli. On immersing one forearm in cold water for four minutes the systolic pressure rose in that arm from 57 to 70, the diastolic remaining below 60. There was no change in the blood pressure in the other arm. This would appear to be a local reflex action.

Ellis and Haynes (1936) found that cold caused the blood pressure to rise in one patient, and that heat caused normal reflex vasodilatation. Ganshorn and Horton (1934) found that the application of cold caused a rise in blood pressure both when sitting and standing. There was failure to respond to cold in the cases reported by Woofter and Deibert (1943) and Young (1941). Stead and Ebert (1941) found that cooling the skin and painful stimuli such as pinching the skin caused vasoconstriction. Jeffers, Montgomery, and Burton (1941) found that these stimuli had no such effect, and recorded a curious result, that heating the legs and right hand caused thermal vasodilatation in the left hand.

The variable response to these stimuli is difficult to explain. Perhaps the lesion, if central, may not involve the centres concerned; or in some persons there may be reflex

paths which do not involve the centre. These reflexes may operate through centres in the spinal cord.

Tachycardia. Although nearly all cases of postural hypotension have a pulse rate that varies but little, and does not accelerate under atropine, there are a few in whom tachycardia occurs on standing up. In Sanders' (1932) case the abrupt increase in rate was due to change in the auricular pacemaker.

MacLean and Allen (1940) noted a pronounced rise in rate in a woman who had developed postural hypotension after an extensive sympathectomy, and in a fairly typical case of postural hypotension in a woman with subacute combined degeneration of the cord. There is no mention of the effect of atropine here. Some increase in rate has been noticed on standing up by Stead and Ebert (1941), and by Jeffers, Montgomery, and Burton (1941). Further information is needed about these exceptions to the general rule, particularly as to the effect of atropine. Possibly some variation in the site of the lesion may be the cause. The effect of atropine is recorded below and agrees with that obtained by most observers; also the effect of adrenalin, ephedrine, paredrine, benzedrine, and pituitrin.

Atropine. With a hypodermic injection of 1/100 of a grain, the patient being recumbent, the mouth was dry after five minutes, but the heart rate remained steady at 84. The blood pressure rose from 85/55 to 115/80. The slight rise in blood pressure is hard to explain. Paralysis of the vagus did not cause any acceleration of the heart due to the unopposed action of the sympathetic. This is in accord with the failure of the heart to accelerate on changes in posture.

Acceleration occurs, however, from the direct effect of sympathetico-mimetic drugs on the heart.

Adrenalin. The effect of 1/1000 adrenalin solution, m. 5 injected hypodermically, the patient being recumbent, was to cause a rise in blood pressure from 130/90 to 155/100 in two minutes, and the heart to accelerate from 88 to 108; while m. 10 caused the blood pressure, recumbent, to rise to 180/120, and provoked an attack of supraventricular tachycardia lasting twenty minutes, with much tremor and pallor. The patient is evidently very sensitive to these sympathetico-mimetic drugs.

A very severe reaction to 5 minims of adrenalin solution was recorded by Korns and Randall (1937), severe cardiac pain being provoked, which had to be relieved by amyl nitrite. The effect is too short and sharp for therapeutic use.

Ephedrine. In view of the possible therapeutic effect by reason of more prolonged action, the effect of half a grain of ephedrine by mouth was noted. The patient was sitting with the arm dependent. After thirty seconds the blood pressure rose from 78/50 to 120/70, the heart rate rising from 84 to 98. At the end of four hours the blood pressure was 120/90 and the heart rate 96.

As far as the sitting posture went, there was considerable improvement, and the patient felt well. The effect while standing was less beneficial. Although after the administration of half a grain by mouth the pressure when lying rose to 170/105 from 148/98 in 35 seconds, the rise on standing was to 96/68 from 62/45 in the same time. After two hours the pressure, recumbent, was 155/105; while the standing pressure was 60/—, the diastolic being unreadable.

Ephedrine stimulates the smooth muscles of the arterioles directly; the effect in this patient, when recumbent, is unusually strong and prolonged considering the dose. It is clear that the vasoconstriction is not adequate to prevent a fall of pressure on standing. But the usual tendency for pressure to rise when recumbent is augmented to a considerable degree. But caution is required with ephedrine, for unpleasant effects have been recorded (Sanders, 1932).

Paredrine. The effect of paredrine was observed. The oral administration of 20 mg. caused the blood pressure to rise from 45/10 to 70/50 in about an hour and a half while standing. Lying, the pressure rose from 80/50 to 135/110 in the same time. It would appear to be less effective than ephedrine.

Benzedrine. The observations show a considerable pressor effect, especially when recumbent. There was also a subjective feeling of improvement. A total of 60 mg. was given in the course of eight hours. The sitting blood pressure rose from 70/40 to 170/120. The

standing pressure rose from 35/20 to 100/70. There was a considerable feeling of elation. The pulse rate rose from 88 to 102. Five hours later the effect had worn off.

The effect of this drug is unusually intense and prolonged, and similar in this respect to the others of this group. A smaller dose of 22·5 mg. given in two hours caused the standing pressure to rise from 60/50 to 105/85; the sitting pressure from 70/54 to 145/115, and the lying pressure from 120/95 to 180/130. The first two doses of 7·5 mg. produced but little effect.

Pituitrin. Stimulating the unstriped muscle of the arterioles caused slight rise in blood pressure, and slight acceleration, as one might expect: 0·3 c.c. caused the blood pressure to rise, when recumbent, from 90/55 to 125/90 in two minutes: the pulse rate rose from 70 to 90.

Sweating. The anhydrosis is sometimes unilateral, as it was in this case, the right side being affected thirteen years before the other. The statement that he had never sweated on his face may be inaccurate, or may indicate that the lesion began quite early in life. Ghrist and Brown (1928) noted unilateral anhydrosis several years before the other symptoms. In Laplace's case (1942) the sweating was intermittent, apparently varying with the blood pressure: when the pressure could be made to rise, as in exercising the muscles of a limb to which a tourniquet had been applied, sweating returned. Korns and Randall (1938) found that when large doses of benzedrine were given sweating returned. There was, however, no response to pilocarpine (1/8 of a grain) given by mouth.

There was a return of sweating in a patient of MacLean and Allen (1940) who was treated by raising the head of the bed; this appeared to be accompanied by improvement in the reaction of the blood pressure to standing. A tendency to increased sweating on one side of the body while sitting still was noted by Riecker and Upjohn (1931).

In nearly all cases the sweat glands, or the autonomic nerve endings in them, respond to pilocarpine. The erratic distribution of the areas of anhydrosis needs further study in orthostatic hypotension. It may be that in the hypothalamus, lesions occur that correspond to certain body areas. The unilateral anhydrosis suggests this, and more detailed delineation of these areas might be profitable. The suggestion that the level of the blood pressure may affect sweating is interesting, but there may be actually improvement in parallel functions.

Impotence. Loss of libido and sexual activity is recorded in almost all the male cases; this has occasionally appeared as quite an early symptom. Benzedrine produced an improvement according to Korns and Randall (1938). As some of the patients have had such diseases as tabes dorsalis the defect may have been due to this cause, apart from the lesion peculiar to hypotension; but as it occurs in others with no apparent lesion of the central nervous system, it may be due to a hypothalamic lesion. Much more information is needed about the pathogenesis of this symptom.

Nature of Postural Hypotension

There is no control of the distribution of the blood in the arterial system. The blood behaves as though the arteries had no vaso-constrictor control. When the patient stands up blood tends to pool below the level of the heart. But Stead and Ebert (1941) have shown that the proportion of the total blood volume contained in the legs in cases of postural hypotension agrees closely with that present in normal persons. The conclusion is that an excessive degree of pooling does not occur. If the normal tendency to pooling be prevented by putting tourniquets on the legs, the brachial pressure does not fall in these patients. In the same way the application of external hydrostatic pressure by standing the patient in water up to the heart will prevent the pressure falling. Stead and Ebert (1941) conclude that the cause of this disorder is an " abnormal response to the pooling of a normal quantity of blood." The nature of this abnormal response has been investigated by these observers by noting that the flow of blood in the hand did not decrease as the pressure fell. This would point to a failure in the compensatory vaso-constriction, which in the normal person prevents a fall in blood pressure on standing up. Jeffers, Montgomery, and Burton (1941) confirmed that the flow of blood in the fingers of a patient with postural hypotension did not decrease on standing up, as it does in normal persons.

The rise in blood pressure which occurs in the arm when the patient is tilted head downwards shows that there is lack of control over the distribution of the blood. The fall in

blood pressure in one arm when the limb is raised, the patient being recumbent, illustrates, in one limb, what occurs in the body as a whole.

Site of the lesion. The peripheral vessels can be made to constrict by the action of vaso-constrictor drugs, so the defect does not lie in their musculature nor in their sympathetic nerve endings. In most cases vaso-constrictor reflexes acting through the sympathetic ganglia, such as may be elicited by painful stimuli, are intact. Changes of temperature in other parts of the body still cause vaso-dilatation or constriction elsewhere.

The failure in postural vaso-constriction is associated with a fixed heart rate in the large majority of cases, as shown by the inability to accelerate under atropine, or when the blood pressure falls. With this are associated anhydrosis and impotence. To account for this triad it seems necessary to look for some central site. Ellis and Haynes (1936), Wooften and Deibert (1943), and Young (1941) have stressed the association of this disease with diseases of the central nervous system, such as tabes dorsalis and encephalitis. The general consensus of opinion seems to be that the hypothalamus is the most likely site. So far there is no post-mortem evidence on the subject. The lesion must vary in extent and site, so that one can account for the exceptional cases in whom there is tachycardia on standing.

Apart from the central site, there are patients in whom there have been lesions of the cord such as hæmatomyelia, syringomyelia, and transection. Here it may be argued that either the afferent paths or the efferent paths might be interrupted. Very extensive sympathectomy may produce a similar result.

Treatment and Prognosis. This is not very satisfactory and at the most is only palliative. Following the observation that the patient was usually better in the latter part of the day, perhaps because some sort of adjustment had been achieved, MacLean and Allen (1940) have advocated sleeping with the head of the bed raised, so that the patient was never really horizontal. In the patient here described this made no difference; but he was unusual in being but little better towards evening in any case.

Bandages and binders are not practical if used so that they really check the tendency to pooling.

Patients seem to have to reduce exertion to a minimum in warm weather, and to avoid standing still. Shifting the feet and shuffling movements (Croll and Duthie, 1935) seem to lessen the tendency to fall in pressure.

Drugs. The vaso-constrictors have a certain value. That they cause a considerable rise in pressure in some cases when recumbent has been shown. In fact, adrenalin tends to be too violent in its action.

In spite of the rise in pressure when the patient is lying down, the fall still occurs when he stands up. But nevertheless, the effect on the patient is less, and the fall may be less severe. They are therefore worth while. The choice seems to lie between ephedrine, paredrine, and benzedrine. For the patient described a combination of benzedrine 5·0 mg. at 8, 9, and 11 a.m., and ephedrine 30 mg. at 1, 3, and 5 p.m., seemed to work best and helped him to get through the day fairly well. It is best to give the benzedrine early, as it seems to induce a feeling of well-being soon in the day and does not cause insomnia. Korns and Randall (1938) gave 80 to 100 mg. of benzedrine in the morning and paredrine 40 mg. every two hours till 2.30 p.m., up to 160 mg. By this means sweating and sexual activity returned.

Prognosis. The disease appears to run a prolonged course. Having reached a certain degree of severity it does not become worse. There is so far no record of fatal results. It would be interesting to know what has happened to those patients described ten years ago or more. In some instances the associated disease of the nervous system may be of a progressive character. Laplace (1942) described a case with a prolonged remission.

Summary

A case of orthostatic or postural hypotension is described.

Observations are recorded on the effects of posture on the brachial blood pressure.

The effects of sympathetico-mimetic drugs are recorded.

The stability of the heart rate under atropine and on changes in posture is noted.

The nature of the defective vasomotor control is discussed and the possible site of the lesion.

Attention is drawn to the associated symptoms of anhydrosis and impotence, which form a triad.

Benzedrine and ephedrine provide palliative relief.

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CARDIOVASCULAR DISEASES IN THE BRITISH ARMY OVERSEAS

BY

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From various Military Hospitals in the Mediterranean Theatre

Received March 1, 1946

The writers of the present communication have, during three years with British Military Hospitals in North Africa, Greece, and Italy, dealt with very large numbers of sick. In a certain period of 27 months, 9824 in-patients came under the charge of one of us (K.S.S.), while during a period of 23 months the other (R.A.M.) has examined 1431 out-patients. As we have both been impressed by the infrequency of cardiovascular disease and disorder, particularly in contrast with the incidence in the First World War, we have undertaken a survey of the number and varieties of these conditions in each of these groups.

Material and Period of Survey

Upwards of 11,000 patients have been observed in more than one hospital, but in no case was the hospital one to which cardiovascular cases were specially directed. During the 8-months' period from April to November 1944 there was another hospital in the vicinity at which electrocardiographic examination was available, but the quarterly returns showed that this caused no alteration of the average incidence of cardiovascular disorders among our patients. Our figures are therefore derived from unselected sources. Moreover, as there is no kind of heart disease or disorder in which climate or other regional variable would be likely to influence incidence in adults, the figures are probably representative of the general incidence in the British Army overseas. Foreign service in itself might be regarded as an influence favouring functional cardiovascular disorder so that our figures are possibly not representative of the British Army as a whole.

The patients with which this survey is specially concerned are those afflicted with primary organic heart disease such as mitral stenosis, or syphilitic aortitis, and those with functional disorders such as effort syndrome or vaso-vagal syncope. A further group necessarily came under consideration; these were the patients with cardiac disorders due to some underlying non-cardiac disease. Conditions under this heading were the acute myocarditis of diphtheria, and the acute left ventricular failure sometimes seen in acute nephritis. Lesions partly arterial or venous, such as trench-feet or thrombo-phlebitis, have been excluded from this survey. Typhus, in spite of its impact upon the cardiovascular system, has also been excluded.

The period which has come under consideration for in-patients is that from July 1, 1943, to September 30, 1945—27 months. The first six months of 1943 were exceptional in that the hospital organization was overburdened with great numbers of battle casualties and the large influx of those sick with malaria and dysentery. These circumstances, although they would lend additional point to our figures, have led us to start the survey from July 1943. The period over which the 1431 out-patients have been seen is from December 1942 to November 1943 and from November 1944 to November 1945.

Observations

The Table shows the numbers of cases of various diseases and disorders occurring in each period of 12 and 15 months. It will be seen that among a total of 9824 in-patients there were only 42 cases of organic cardiovascular diseases and 23 cases of functional circulatory

disorders. The total of 65 patients represents an incidence of 0·66 per cent. There were, in all, 5 patients with cardiac disorders secondary to diphtheria or nephritis, and if these be included the total is 70 patients, an incidence of 0·71 per cent.

An analysis of the 42 patients with organic disease shows rather more than half (23) to be hypertensive or degenerative, rather less than a third (13) rheumatic, 3 syphilitic, and 1

TABLE

INCIDENCE OF CARDIOVASCULAR DISORDERS AT BRITISH MILITARY HOSPITALS IN THE MEDITERRANEAN THEATRE

Diagnosis	In-patients (9824)			Out-patients (1431)		
	July 1, 1943, to June 30, 1944	July 1, 1944, to Sept. 30, 1945		Dec. 1942 to Nov. 1943	Nov. 1944 to Nov. 1945	
Effort syndrome	9	2		17	4	
Vaso-vagal syncope ..	4	4		0	0	
Paroxysmal tachycardia ..	2	0		0	0	
Left mammary pain ..	0	2		3	2	
Total " functional " ..	15	8	=23	20	6	=26
Mitral stenosis	3	2		2	1	
Aortic valve disease ..	1	4		0	0	
Mitral and aortic disease ..	1	1		1	0	
Rh. pericarditis and carditis	0	1		0	0	
Syphilitic aortitis	0	2		1	1	
Aortic aneurysm	0	1		0	0	
Hypertension	6	9		3	1	
Effort angina	0	2		0	0	
Cardiac infarction	0	4		1	0	
Arteriosclerosis	2	0		0	0	
Congenital heart disease ..	0	1		1	0	
Pericarditis (non-rheum.) ..	0	2		0	0	
Total " organic " (primary)	13	29	=42	9	3	=12
Diphtheritic myocarditis ..	1	2		—	—	
Left ventricular failure in nephritis	2	0		—	—	
Total " organic " (secondary)	3	2	=5	—	—	—
Total all cardiovascular—		In-patients	=70	Out-patients	=38	
Total all patients of same period		(I.P.)	=9824	(O.P.)	=1431	
Cardiovascular cases: percentage of total		(I.P.)	=0·7	(O.P.)	=2·7	

congenital. The remaining 2 were cases of non-rheumatic pericarditis. Of the 23 functional cases, half (11) suffered from effort syndrome, 8 from vaso-vagal syncope, 2 from paroxysmal tachycardia, and 2 from left mammary pain.

A further analysis of these figures in terms of incidence earlier or later in the 27 months is of interest. A dividing line at June 30, 1944, gives a total of 5740 patients under review before and 4084 after this date. During the earlier period there were 15 cases of functional and 8 of organic disease; whereas during the later period there were only 8 cases of functional disorder compared to 29 patients with organic disease.

The second part of the table shows the occurrence of cardiovascular disorders among out-patients during two periods; the first from December 1942 to November 1943, the second from November 1944 to November 1945. In the first period, of a total of 1125 cases, only 29 (2·5 per cent) suffered from cardiac syndromes. In the second period, the incidence was 9 out of 306 patients (3·0 per cent). This total of 38 patients represents a percentage of 2·7 per cent. The difference in the total numbers seen in the two periods is due to the fact that during the first period a number of Infantry and General Reserve training depots were in the neighbourhood.

In the first period, 20 were functional and 9 organic, and in the second period, 6 were functional and 3 organic—thus in each group two-thirds of the patients had functional disorders. Clearly the somewhat higher incidence of cardiac disorders in out-patients as compared with in-patients is accounted for by the greater numbers of functional disorders not requiring admission in this class of patient.

Comments and Discussion

The most remarkable thing about the figures in general is that they are so low. More conspicuous still is the infrequency of functional cardiovascular disorders; a total of 49 among 11,255 in- and out-patient sick is astonishingly small when it is remembered that in the war of 1914–18 disturbance of the cardiovascular system was of major importance—one case being observed for every four men wounded—and the group as a whole being second in dimensions only to pulmonary diseases among medical disorders (Lewis, 1940).

Lewis also states that 70,000 men had reported sick and been classed as cardiovascular by the summer of 1918. Among pensioners were 44,000 cases of "effort syndrome." The official history of the Great War gives 36,569 as the number of men discharged from the Army and Navy, up to May 1918, on account of cardiovascular disorders; it also claims that the true numbers of those reporting sick with cardiac symptoms must have been much in excess of Lewis' calculation of 70,000.

That functional disorders exceeded the organic during the war of 1914–18 was also indicated by the figures of Parkinson (1916). Among 90 consecutive soldiers reporting sick with symptoms suggestive of heart disease at a Casualty Clearing Station 28 had organic disease (almost all valvular) compared with 40 with "so-called soldier's heart." The remaining 22 cases were non-cardiac.

Wood (1941), investigating these cases at an Effort Syndrome Unit, referred to the fact that there were but two special centres in England and one in Scotland; working at the largest of these he had dealt with no more than 700 during the first 20 months of the war. In the Middle East Force, from 1941 onwards, all cases of effort syndrome were sent to one centre for disposal. At this centre 338 cases were observed by Hill and Dewar (1945) between July 1941 and February 1945.

The few cases of functional disorder dealt with in hospital in the present series show that medical officers are alive to the fact that patients with symptoms of this kind do not respond well to treatment as in-patients, and may be even the worse for it. Doubtless, the increased understanding of the psychogenic basis of this disorder has enabled doctors, at all stages in the soldier's career, to avoid fanning the spark of their malady into the full flame of a doctor-made disorder. The diminishing number of these cases with the passage of time may be due to the fact that the initial conditions of active service would be more likely to produce this type of psychosomatic response, and also to the increasing awareness of medical officers of the correct disposal of such cases as they developed.

To the small number of patients with cardiac neurosis must be added a considerable number who broke down with its counterpart in other systems. It may be that the numbers treated for "exhaustion" at forward centres and invalided on the score of anxiety state and psychopathic personality far exceeded any corresponding groups in the war of 1914–18.

The rising incidence of organic disease contrasted with the diminishing frequency of the functional; although the second (later) period under review comprised substantially fewer patients (4084 to 5740) there was a more than threefold increase in cases of organic cardiovascular disease. This trend suggests that with the prolongation of the war to three, four, and five years, hypertensive and degenerative changes had time to develop as a result of continuing stress and strain in those constitutionally prone to them; at the same time, the army of this later stage will have comprised a greater proportion of men in the higher age-groups.

A few general comments follow.

(1) The remarkable low incidence of cardiovascular disorders in the Army (less than 7 per 1000 of all sick admitted to hospital) reflects much credit on Recruiting Medical Boards who succeeded in eliminating at this stage the vast majority of patients with organic cardiovascular disease and to a large extent weeding out those prone to effort syndrome and other

neuro-circulatory upsets. Analysis of effort syndrome cases of 1914–18 showed that 43 per cent had had symptoms on enlistment (Lewis, 1940).

(2) A total of 17 cases of rheumatic heart disease was a very small number. These cases are generally not hard to detect at routine recruiting examinations. The cases encountered in this series no doubt included some whose signs were very slight two or three years previously when they joined up. The physical stress of army life and campaigning might be expected to accelerate the natural diminution of the cardiac reserve. A majority of the patients with rheumatic valvular disease presented with gradually increasing breathlessness on exertion.

(3) Apart from the low incidence of rheumatic heart disease, the incidence of acute infective polyarthritis of all types was astonishingly low when the living conditions of the men are remembered (only 62 cases, or 0·6 per cent of all in-patients). Both in the winter and spring of 1943 in North Africa, and in the same seasons in Italy in 1944, the front-line soldiers were subjected to prolonged exposure to wet and cold. Among the very few acute arthritic illnesses encountered there was only one case in which valvular disease developed in a heart believed to be previously healthy. In this man of 24 years acute polyarthritis was succeeded by pericarditis and thereafter an aortic diastolic murmur was heard for the first time.

(4) Only two cases of congenital disease were encountered. The first was an unobtrusive one, and a condition (dextrocardia) that might easily be passed over among large numbers of examinees, and it might be added, appropriately so. The second was pulmonary stenosis with few signs that may well have progressed under active service conditions.

(5) Certain cardiac disorders secondary to diseases which are not uncommon have a special significance in active service conditions.

(*a*) *Diphtheria.* This disease is common in the army overseas. Fortunately, acute diphtheritic myocarditis is a rare event owing to the insistence among medical officers on large and early dosage with anti-diphtheritic serum even in suspected cases, and appreciation of the paramount necessity for at least four weeks rest in bed. Special risks exist in that diphtheritic infection of septic sores or abrasions carry the same threat to the heart as faucial infections but are more insidious in their development of circulatory and neuritic complications and are more likely to escape correct diagnosis. For example, during active operations a patient may be admitted for treatment of injuries the severity and priority of which detract attention from an indolent painless sore in which diphtheritic infection has supervened, until myocarditis or neuritis are far advanced.

(*b*) *Acute nephritis.* It is well known that acute left ventricular failure with paroxysmal nocturnal dyspnœa sometimes develops in the course of acute nephritis, particularly when the hypertension is conspicuous or sustained. This complication has twice been encountered in the present series, in patients with acute nephritis whose principal complaint was waking in the night short of breath. The onset with this symptom might be related to the more strenuous life of the average soldier compared with the average civilian.

(6) During the period under review the number of in-patients with lobar or bronchopneumonia was 100. It is known from morbid histological studies that myocarditis may complicate these diseases (but not primary atypical pneumonia). However, in no case was there evidence either of myocarditis or of right heart failure. Nor did secondary pericarditis ever develop. This result is surprising when the conditions under which they were taken ill, and the consequent likelihood of a severe infection, are borne in mind.

(7) Certain unusual conditions may be contingent on active service. For example, in 1943 in North Africa when prophylactic mepacrine was first instituted, a medical officer developed auricular fibrillation in the course of gastro-enteritis that followed the third dose of 0·2 g., the doses being at 4-day intervals. After some hours the arrhythmia disappeared. The patient had a healthy heart, and he has had no such disturbances in the two years that have since elapsed.

SUMMARY

An investigation has been made of the incidence of cardiovascular disorders among British soldiers overseas.

A survey of 9824 consecutive admissions to a Medical Division, and of 1431 consecutive soldiers attending an out-patients' clinic, has been made.

Among the 9824 in-patients there were 70 cases of functional or organic cardiovascular disorder, an incidence of only 0·71 per cent. The organic disorders were about twice as frequent as the functional. During the later part of the 27-months' period, there was an increasing ratio of organic to functional disorder.

A total of 38 patients with cardiovascular disorders were observed among the 1431 out-patients (2·7 per cent). Approximately two-thirds of these patients had functional conditions and one-third organic lesions.

Effort syndrome never represented an important medical disability owing to (i) efficient selection by Recruiting Medical Boards, and (ii) better understanding of the appraisal and disposal of cases at their inception by army medical officers. The infrequency of effort syndrome contrasted sharply with its high incidence in the war of 1914–18.

Heart conditions have very rarely been initiated by rheumatism acquired on active service. Among many cases of pneumonia there were no examples of myocarditis.

The special significance of diphtheria and nephritis as causes of cardiovascular disorders in military practice is discussed.

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THE ACTION OF MAGNESIUM ON THE HEART

BY

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Received May 12, 1945

Although it has been repeatedly established both in man and in animal experiments that magnesium has a depressant action on the heart, there is no general agreement about the mechanism of this action, and there are few reports dealing directly with the clinical application of its cardio-inhibitory properties. Zwillinger (1935) studied the effect of magnesium sulphate on paroxysmal tachycardia, auricular fibrillation, flutter, and extrasystolic arrhythmia; the paroxysms of tachycardia stopped immediately after the intravenous administration of the drug; extrasystoles were usually abolished; no effect, however, was noticed in auricular fibrillation and flutter. Rothberger and Zwillinger (1936) showed experimentally that magnesium salts in large doses depress conduction, and depress or abolish abnormal impulse production: they succeeded in combating ventricular tachycardia produced by barium chloride or strophanthin. Miller and van Dellen (1938) conducted cardiographic studies in dogs that had been given magnesium sulphate intravenously, and observed a delay in A-V and intraventricular conduction time. Smith, Winkler, and Hoff (1939) reported a sequence of cardiographic changes in the unanæsthetized dog during continuous intravenous administration of magnesium sulphate. They showed that intra-cardiac conduction was depressed in all its elements. After a transient initial tachycardia, bradycardia appeared, and there was a progressive increase in the P–R interval as the concentration increased, until A-V block of various grades and widening of QRS appeared. If the concentration was raised sufficiently, cardiac arrest resulted. Except for the initial tachycardia, similar results were obtained in cats. In the authors' own words—" the cardiac arrest which always occurs if the magnesium concentration is pushed high enough cannot be explained as the result of this depression of conduction, since in most instances the last beats showed a well defined and vigorous systole. For an adequate explanation of this final arrest it is necessary to assume a more direct toxic action of magnesium on the myocardium itself." Bernstein and Simkin (1939) observed only minor changes in the human cardiogram following the intravenous injection of 10 to 20 c.c. of a 10 per cent solution of magnesium sulphate in both cardiac and non-cardiac subjects. These changes consisted of variations in the amplitude of the QRS and T waves. There were no changes in the heart rate or the P–R interval. Boyd and Scherf (1943) recommended magnesium sulphate as a useful therapeutic procedure in paroxysmal tachycardia; using 20 c.c. of a 20 per cent solution they succeeded in terminating each of eight attacks. In one of the paroxysms reported by Decherd and Herrmann (1944) magnesium sulphate, injected intravenously to measure the circulation time, stopped the tachycardia immediately. In a recent report Pines *et al.* (1944) produced further evidence of the cardio-inhibitory property of magnesium sulphate, and showed that the addition of magnesium sulphate to the intravenous or intracardiac injection of a lethal dose of mercurial diuretic prevents ventricular fibrillation and death of the dog.

Present Investigation

The 26 cases included in this study were in-patients of the Newcastle General Hospital under the care of Professor W. E. Hume: they comprise 13 with paroxysmal tachycardia, 9 with auricular fibrillation, 5 of which also showed extrasystoles, and 4 with purely extra-

systolic arrhythmia. Three of the cases of paroxysmal tachycardia might have been regarded as instances of auricular flutter, but they conform to the definition of paroxysmal tachycardia given recently by Evans (1944). Some of the cases of paroxysmal tachycardia and auricular fibrillation were included in the material of a previous study (Szekely, 1944), but none of the cases analyzed here in detail and none of the cardiograms have been reported before. Ten cases with sinus rhythm were also studied with special reference to the effect of magnesium on the rate, the P–R, QRS, and Q–T intervals. In each instance magnesium sulphate was given intravenously, the dose being 20 c.c. of a 20 per cent solution unless stated otherwise.

Case 1. A woman, aged 67, was admitted to hospital in October, 1942, with congestive heart failure and auricular fibrillation. Treatment with digitalis was started at once (digitaline Nativelle, 1/600 of a grain, six times daily). Four days later, she was found to have paroxysmal tachycardia at a rate of 168 a minute (Fig. 1). Digitalis was discontinued and 10 c.c. of a 20 per cent solution of

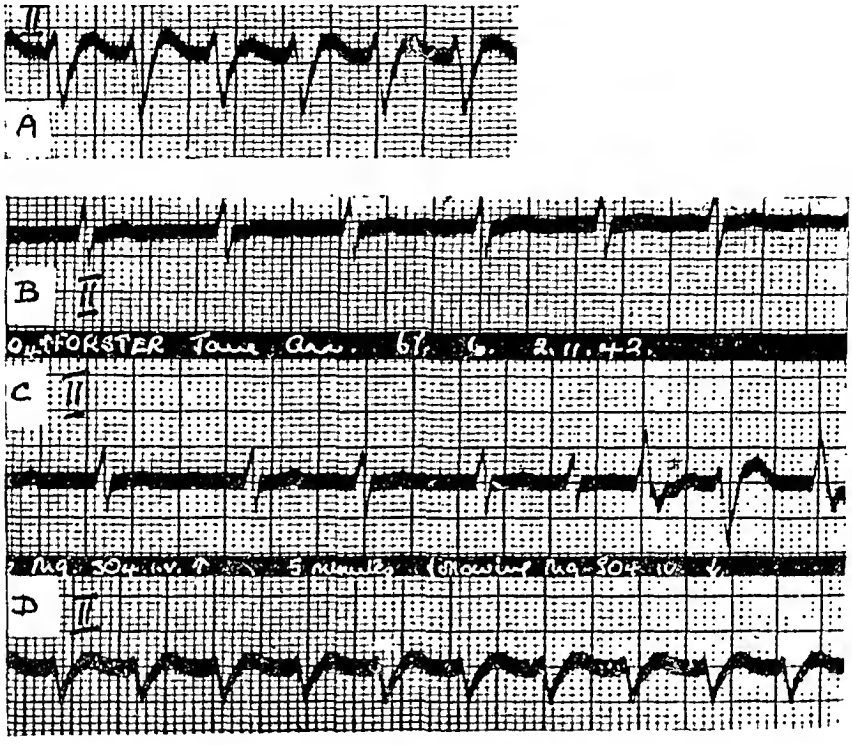

FIG. 1.—Case 1. Paroxysmal tachycardia occurring during auricular fibrillation. (A) Before, (B) Immediately after, (C) 3 minutes after, and (D) 5 minutes after injection of magnesium sulphate. This and subsequent figures have been reduced to five-sixths.

magnesium sulphate were given intravenously. The tracings taken immediately after, and three and five minutes after the injection are reproduced in Fig. 1; they show immediate cessation of the tachycardia and restoration of auricular fibrillation. After three minutes extrasystoles appeared and paroxysmal tachycardia recurred. A second injection of magnesium sulphate, ten minutes later, had the same effect, but this time the tachycardia was arrested for about seven minutes. As the tachycardia recurred and persisted, quinidine sulphate was started by mouth. After three doses each of 5 grains at two-hourly intervals, auricular fibrillation reappeared. Quinidine was then continued, 3 grains daily. Two days later, digitalis was restarted and after two doses of 1/600 of a grain of digitaline Nativelle a rapid regular rhythm developed, presumably paroxysmal tachycardia as before, and the patient died shortly after. Autopsy revealed a moderate degree of diffuse coronary sclerosis with some myocardial fibrosis.

Case 2. A man, aged 59, entered hospital with hypertensive heart failure. He showed the Wolff-Parkinson-White syndrome. The attacks of tachycardia usually lasted for more than twenty-four hours. Intravenous magnesium sulphate terminated one of the paroxysms within five minutes (Fig. 2). As the effect of magnesium is usually immediate (Boyd and Scherf, 1943), it is doubtful whether the disappearance of the tachycardia in this case can be attributed to the drug.

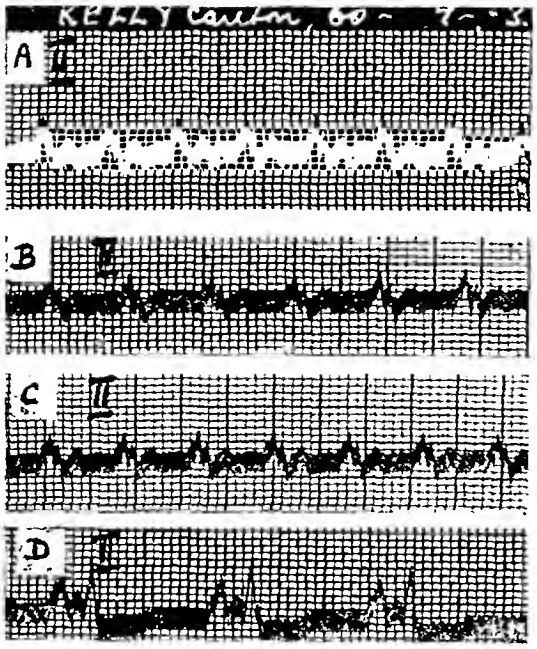

FIG. 2.—Case 2. Paroxysmal tachycardia in case showing Wolff-Parkinson-White syndrome. (A) Before, (B) Immediately after, (C) 2 minutes after magnesium sulphate; no change, and (D) 5 minutes after, showing return of original rhythm.

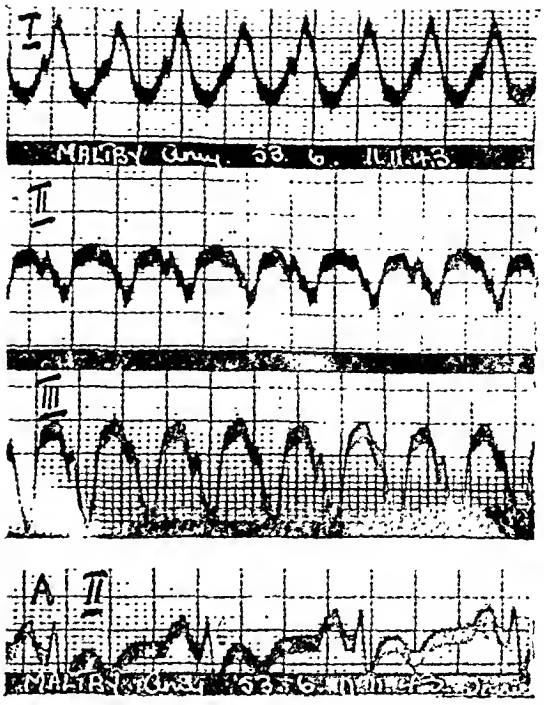

FIG. 3.—Case 3. Mitral stenosis and hypertension. Above, limb leads showing paroxysmal tachycardia, rate 216 a minute. (A) Immediately after magnesium sulphate; sinus rhythm restored.

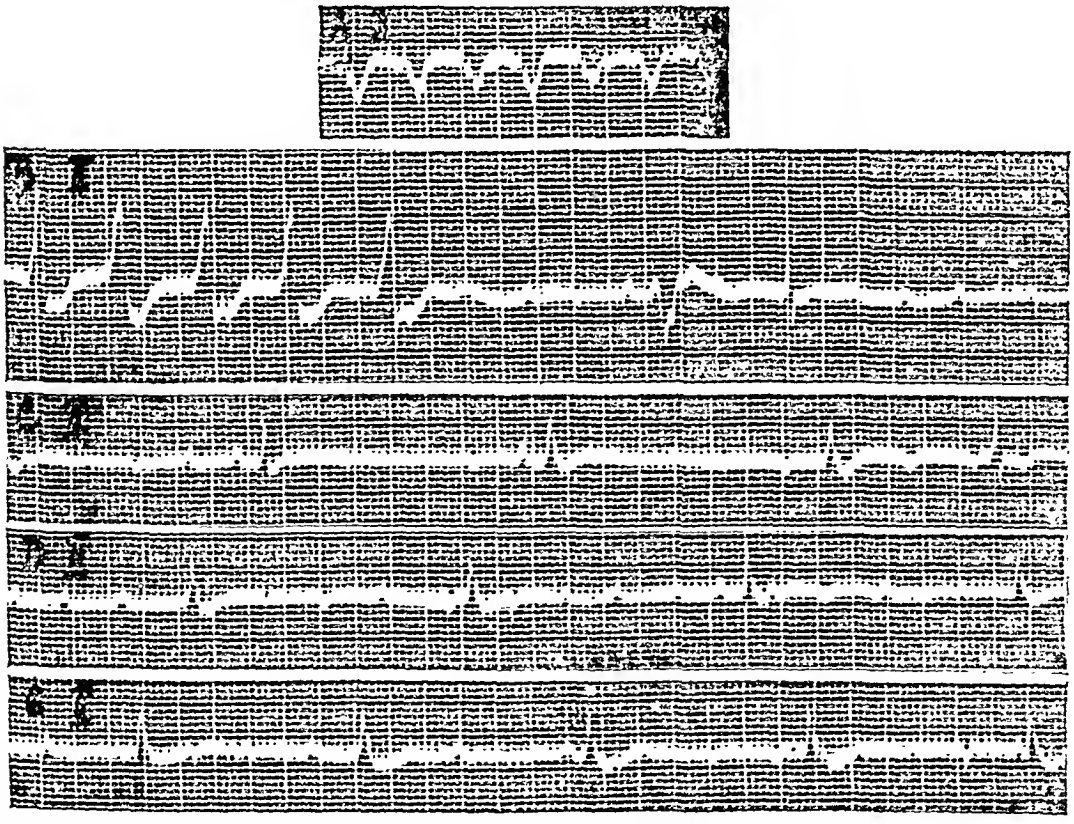

FIG. 4.—Case 4. (A) Before magnesium injection, shows paroxysmal tachycardia, rate 186 a minute. (B), (C), and (D) Continuous strips of lead II after injection. (G) 12 seconds after (D); described in text.

Case 3. A woman, aged 53, was admitted complaining of palpitation. She had taken digitalis for a week before admission. The heart rate was rapid and regular, due to paroxysmal tachycardia, probably ventricular in origin, rate 216 a minute (Fig. 3). The paroxysm was terminated by an intravenous injection of magnesium sulphate and sinus rhythm was restored (Fig. 3). In this case, the effect of magnesium was permanent, and the tachycardia did not recur. During normal rhythm the diagnosis of mitral stenosis and hypertension was established. The patient was discharged two weeks later in a satisfactory condition.

Case 4. A man, aged 74, was admitted with hypertensive heart failure. He had a regular rhythm, rate about 100 a minute. As he did not respond to rest and mercurial diuretics, treatment with digitalis was started. After six days he developed a rapid, regular paroxysmal tachycardia, rate 186 a minute (Fig. 4, A), and digitalis was discontinued. The intravenous injection of 10 c.c. of a 20 per cent solution of magnesium sulphate was followed by a transient change in the shape of the ventricular complexes, but there was no appreciable change in the rate. A few hours later, the same dose of magnesium sulphate was repeated and resulted in immediate changes (Fig. 4, B, C, D, G). After a short run of ventricular tachycardia, rate about 125 a minute, complete A-V dissociation appeared—A., 210; V., 38 gradually increasing to 50. There was variation in the shape of the auricular complexes and alternation of the cycle length. The slow ventricular rate persisted for about eighteen hours, then again rose to about 180 a minute. The patient died shortly after. No autopsy was done.

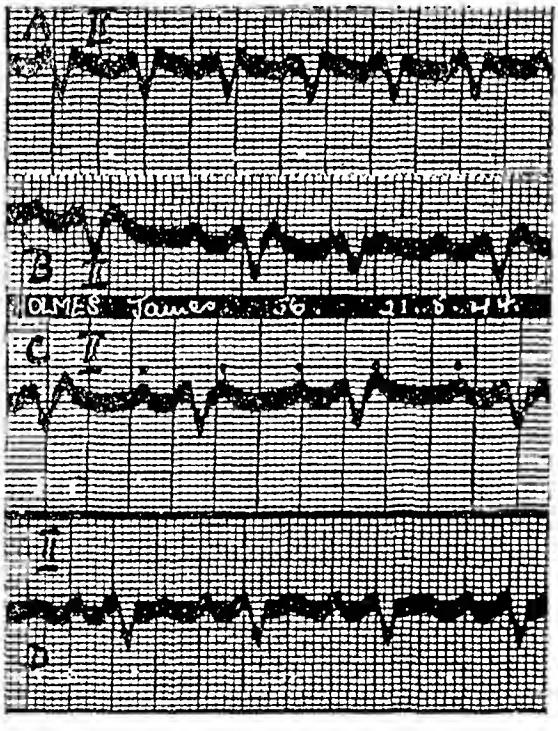

FIG. 5.—Case 5. (A) Paroxysmal tachycardia and probably 2 : 1 A-V block. (B) Immediately after injection of magnesium; 2 : 1 A-V block, auricular rate 170. (C) 3 minutes after; no change. (D) 20 minutes after; sinus rhythm with original bundle branch block pattern.

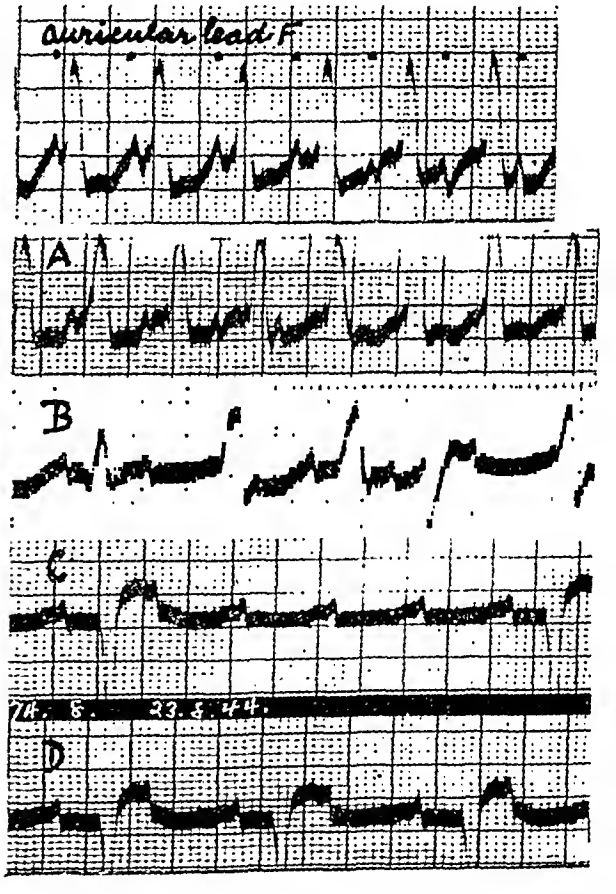

FIG. 6.—Case 6. Auricular chest lead. Upper tracing. Paroxysmal tachycardia with A-V block, dots denote P waves; auricular rate 170, ventricular rate slightly slower. (A) During injection of magnesium; auricular rate 186. (B) Immediately after; auricular rate 170, multifocal ventricular beats. (C) 2 minutes after; auricular rate 150, ventricular rate 30. (D) 3 minutes after; auricular rate 150, ventricular rate 75.

Case 5. A man, aged 56, was admitted to hospital on April 28, 1944, with hypertensive heart failure. He had a large heart, triple rhythm, and left bundle branch block. Treated with digitalis and mercurial diuretics, he improved, but on May 25 his heart rate increased suddenly—paroxysmal tachycardia with 2 to 1 A-V dissociation; auricular rate 340 a minute (Fig. 5, A). Digitalis was discontinued, and the magnesium sulphate was given intravenously. The tracings taken immediately and at intervals of three and five minutes after the injection showed 2 : 1 A-V block, auricular rate about 170 a minute (Fig. 5, B, C). The tracing in Fig. 5, D, taken twenty minutes after the injection, shows sinus rhythm and the original bundle branch block pattern. There was no recurrence of the tachycardia and the patient was discharged ten days later in a satisfactory condition.

Case 6. A man, aged 74, entered the hospital with congestive heart failure. He had an enlarged heart with normal blood pressure and regular rhythm. Four days after admission the heart rate suddenly increased and Fig. 6 showed paroxysmal tachycardia with A-V dissociation, which is clearly shown in the auricular lead. The auricular rate was 170 a minute and the ventricular rate slightly slower. The intravenous injection of magnesium sulphate resulted in only slight changes in the auricular rate, but greater changes in the ventricular rate (Fig. 6, A, B, C, D). After a slight initial rise the auricular rate fell to 150 a minute. The ventricular rate fell to about 30 a minute and then rose to 75 a minute, this rate persisting until the death of the patient three days later. Unfortunately no record was taken before the onset of the tachycardia, so that it is impossible to say what the original rhythm was.

Case 7. A man, aged 23, was first seen in April 1942, and again in November 1944, with mitral stenosis and congestive failure, with normal rhythm. Shortly after admission, paroxysmal tachycardia was recorded, ventricular rate 176 (Fig. 7). Within a few minutes, the deflection of the string changed and lead III, recorded five minutes after the first curve, showed an increased widening of QRS without any change in rate (Fig. 7, A). Magnesium sulphate was then given intravenously ; a curve taken immediately showed no change (Fig. 7, B); after 1½ minutes the QRS returned to its original form (Fig. 7, C); after 2½ minutes sinus rhythm was recorded (Fig. 7, D), and there was no recurrence of tachycardia up to the patient's death six days later. No autopsy was obtained.

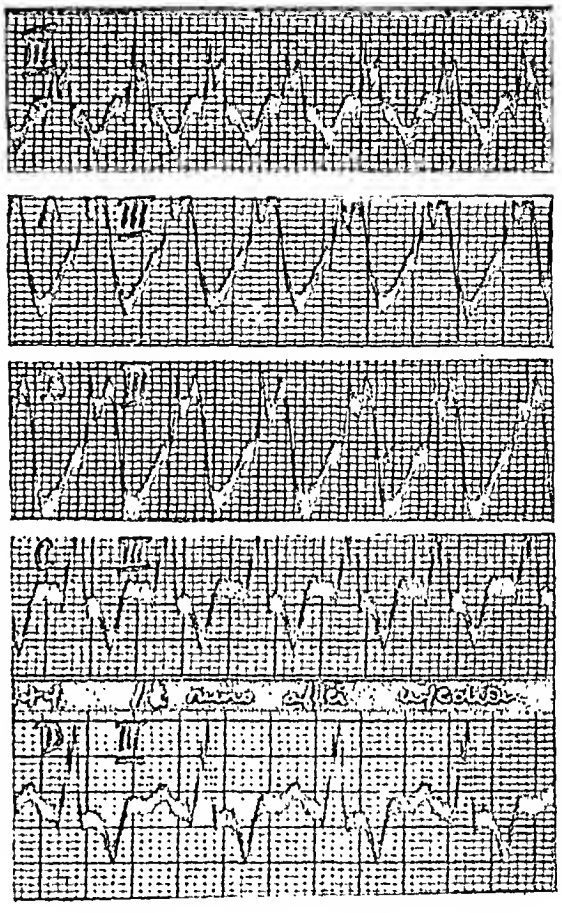

FIG. 7.—Case 7. Lead III. Upper tracing ; paroxysmal tachycardia, ventricular rate 176 ; probably 2 : 1 A-V block. (A) Spontaneous change of QRS. (B) Immediately after magnesium ; no change. (C) 1½ minutes after ; QRS returned to original form. (D) 2½ minutes after; sinus rhythm restored.

Case 8. A man, aged 39, had coronary occlusion with hemiplegia and *Streptococcus viridans* septicæmia. His initial cardiogram showed changes characteristic of anterior myocardial infarction. He died two months after admission and the diagnosis was confirmed at autopsy. Five days prior to death the rhythm changed to auricular fibrillation. About four hours later, a regular tachycardia, auricular rate 500 a minute, was recorded (Fig. 8). Intravenous injection of magnesium sulphate slowed the auricular rate to 300 and the ventricular rate to 150 a minute (Fig. 8, A, B, C). The original rate recurred the following day and persisted until the patient's death.

Case 9. A woman, aged 62, was admitted in 1944, with hypertensive heart failure and left hemiplegia. The cardiogram showed paroxysmal tachycardia with 2: 1 A-V block (Fig. 9, A), auricular rate 320 a minute. Magnesium sulphate intravenously increased the A-V block (Fig. 9, C); 4 : 1 A-V block persisted for an hour, when the original 2:1 block reappeared and persisted until death three days later. Autopsy refused.

Case 10. A woman, aged 51, had been seen for several years with rheumatic heart disease and auricular fibrillation. She died in hospital and autopsy confirmed the diagnosis. During her last three years she had practically never been without digitalis. On one occasion extrasystolic bigeminy was recorded (Fig. 10, A). After an injection of magnesium sulphate the extrasystoles were not completely abolished but their voltage was reduced (Fig. 10, B and C); the voltage of the normal ventricular complex was unaffected. This demonstrates the depressant action of magnesium on ectopic centres, while the normal complexes remain unchanged. The duration of this effect was not observed.

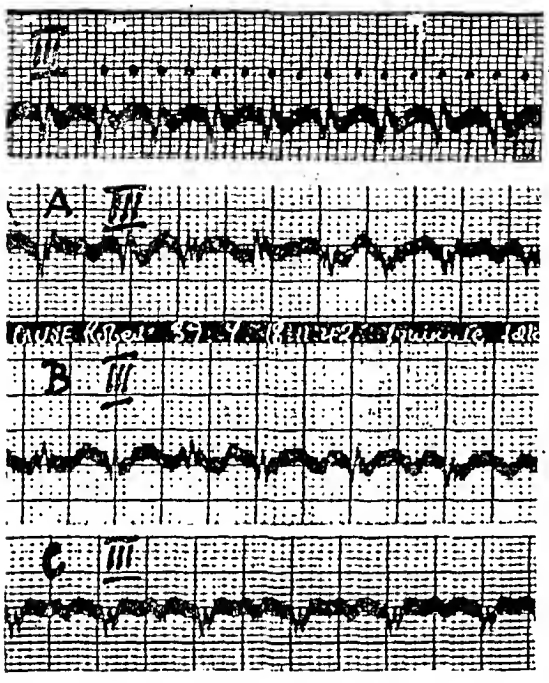

FIG. 8.—Case 8. Coronary occlusion. Upper tracing. Auricular tachycardia with 2 : 1 block, auricular rate 500. (A) 1 minute after magnesium ; variable A-V block. (B) 2 minutes after ; auricular rate 300, variable A-V block. (C) 4 minutes after; auricular rate 300, 2 : 1 A-V block.

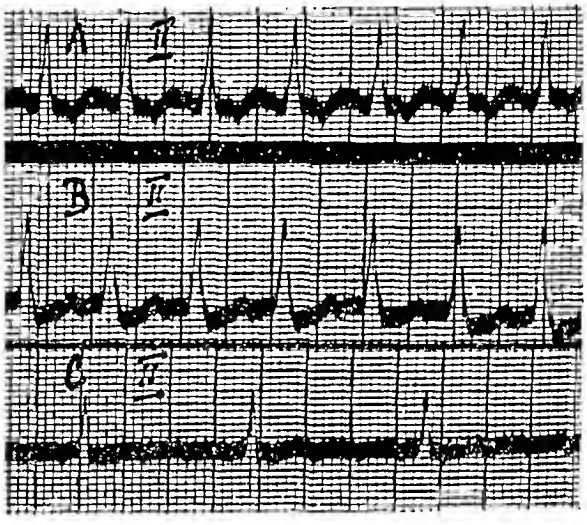

FIG. 9.—Case 9. (A) Auricular tachycardia with 2 : 1 block, auricular rate 320. (B) During injection of magnesium ; change in shape of auricular waves. (C) Immediately after ; ventricular rate halved.

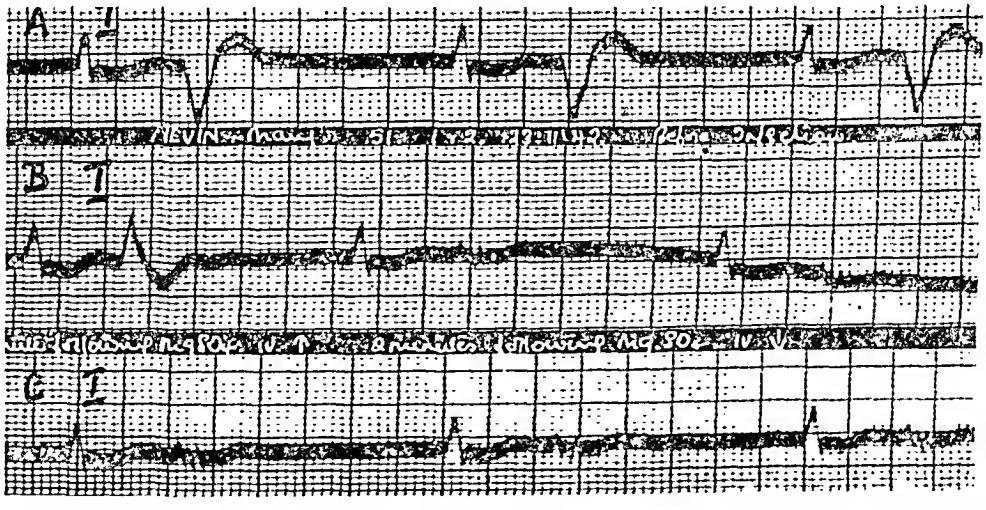

FIG. 10.—Case 10. (A) Auricular fibrillation and extrasystolic bigeminy in a digitalized patient. (B) and (C) 1 and 2 minutes respectively, after injection of magnesium. Decrease in voltage of extrasystolic beat. Voltage of normal complex remains unchanged.

Case 11. A woman, aged 77, was admitted in 1944 with congestive heart failure. The rhythm was regular. Though there was no history of cardiac pain, the low blood pressure and the chest lead cardiogram suggested anterior myocardial infarction. She was given digitalis and mercurial diuretics, and improved; after three weeks treatment extrasystolic bigeminy and 2 : 1 A-V block was recorded (Fig. 11). After an intravenous injection of magnesium sulphate the extrasystoles were completely abolished, and did not recur; the patient was discharged ten days later in a satisfactory condition.

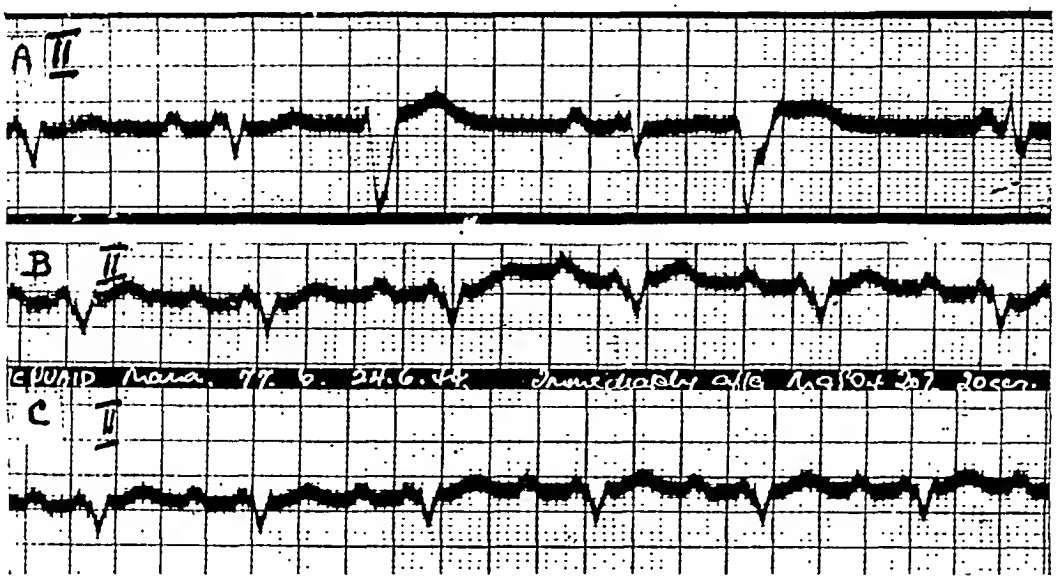

FIG. 11.—Case 11. (A) Extrasystolic bigeminy and 2 : 1 A-V block due to digitalis. (B) Immediately after magnesium and (C) 2 minutes after : sinus rhythm with prolonged P–R ; extrasystoles abolished.

DISCUSSION

The findings confirm the views of previous investigators that magnesium has a depressant action on the heart muscle. The results obtained in paroxysmal tachycardia are summarized in Table I. Of 13 cases, 9 were affected by magnesium, and in 5 of them (Cases 2, 3, 5, 6, and 7) the effect appeared to be lasting; in 4 of them sinus rhythm was restored, and in the fifth case, though the ventricular rate was much reduced, the auricular rate was only slightly slowed, and the A-V dissociation, originally present, persisted. In 4 (Cases 1, 4, 8,

TABLE I

THE EFFECT OF MAGNESIUM ON PAROXYSMAL TACHYCARDIA

Case Number	Underlying heart disease	Auricular rate	Ventricular rate	Duration of effect	Rhythm after injection of magnesium
1 (Fig. 1)	Coronary sclerosis	?	Decreased	3 and 7 minutes	Auricular fibrillation
2 (Fig. 2)	Hypertension	Decreased	Decreased	Lasting	Sinus rhythm
3 (Fig. 3)	Mitral stenosis and hypertension	Decreased	Decreased	Lasting	Sinus rhythm
4 (Fig. 4)	Hypertension	Increased ?	Decreased	18 hours	A-V block
5 (Fig. 5)	Hypertension	Decreased	Decreased	Lasting	Sinus rhythm
6 (Fig. 6)	Coronary sclerosis	Decreased	Decreased	Lasting	A-V block
7 (Fig. 7)	Mitral stenosis	Decreased	Decreased	Lasting	Sinus rhythm
8 (Fig. 8)	Coronary thrombosis	Decreased	Decreased	24 hours	2 : 1 A-V block
9 (Fig. 9)	Hypertension	Unchanged	Decreased	1 hour	4 : 1 A-V block
12	Nil	Unchanged	Unchanged	—	Unchanged
13	Nil	Unchanged	Unchanged	—	Unchanged
14	Mitral and aortic disease	Unchanged	Unchanged	—	Unchanged
15	Nil	Unchanged	Unchanged	—	Unchanged

and 9) the effect was transient, ranging from three minutes to twenty-four hours. In Case 1 the basic rhythm was auricular fibrillation, and this recurred both times the tachycardia was terminated by magnesium. In Case 4, A-V dissociation was present before magnesium was given; after the injection, the auricular rate appeared to be quicker, and there was a marked alternation of the cycle length; the ventricular rate showed a fall. In Cases 8 and 9 the injection resulted in a temporary increase in the A-V block. Magnesium failed to produce any changes in rhythm in the following 4 cases. A male, aged 63, with nodal tachycardia and no underlying structural disease in the heart, whose tachycardia responded to carotid sinus pressure. A male, aged 36, with auricular tachycardia but no structural disease of the heart, whose tachycardia was terminated by digitalis. A female, aged 17, with mitral stenosis and aortic regurgitation, but free from cardiac enlargement or failure; paroxysmal auricular tachycardia stopped after oral digitalization. A male, aged 50, who had auricular tachycardia with 2: 1 A-V block, emphysema, and chronic bronchitis; digitalis first resulted in an increase of the A-V block, and later the tachycardia was replaced by sinus rhythm. Clinically, the interesting feature was the presence of advanced heart disease usually with congestive heart failure in the cases that responded to magnesium, even if the effect was a temporary one, and the absence of these findings in the cases that failed to respond to magnesium. Three of the latter showed no evidence of structural heart disease, and in the fourth there were no signs of heart failure though the heart showed structural changes. The significance of this observation is uncertain as yet, but the question may be usefully discussed in relation to the cardiac action of potassium. Though there is some evidence that potassium may be antagonistic to magnesium (Hirschfelder, 1929; Rothberger and Zwillinger, 1936), there are numerous reports (Ringer, 1882; Sampson and Anderson, 1930; Wiggers, 1930; Winkler, Hoff, and Smith, 1938; Thomson, 1939; Stewart and Smith, 1941; Keith, Osterberg, and Burchell, 1942; Finch and Marchand, 1943; Sampson, Alberton, and Kondo, 1943; Keith, Burchell, and Baggenstoss, 1944) suggesting that the cardio-inhibitory action of potassium is in many respects strikingly similar to that of magnesium. Further, it has been shown that the potassium content of the heart muscle of patients dying of congestive heart failure is diminished (Harrison, Pilcher, and Ewing, 1930; Sampson and Anderson, 1930).

Potassium salts have been used to abolish paroxysmal tachycardia and ectopic beats (Sampson and Anderson, 1930), and it has been suggested that potassium is more effective in this respect when the heart muscle is damaged than when it is healthy. This is ascribed to the low potassium content of the myocardium in heart failure. It is possible that the effect of magnesium in paroxysmal tachycardia depends similarly on the magnesium content of the heart muscle.

Sampson and Anderson (1930, 1932) and Sampson, Alberton, and Kondo (1943) showed that ectopic beats caused by digitalis could always be abolished by potassium, whereas other forms of ectopic beat responded less frequently. There is a loss of potassium from the heart muscle in digitalis intoxication (Sampson, Alberton, and Kondo, 1943). Like potassium, magnesium may be effective in digitalis intoxication (Zwillinger, 1935), and it may be more effective in abolishing ectopic beats due to digitalis than those otherwise caused (Zwillinger, 1935; Herles, 1937; Boyd and Scherf, 1943). The findings given in Table II suggest that magnesium is more likely to affect extrasystoles due to digitalis than other varieties. However, reports dealing with the relation between magnesium and digitalis are contradictory, for Miller and van Dellen (1941) found that magnesium did not counteract digitalis intoxication in dogs. Neither potassium nor magnesium has any effect on the rhythm in auricular fibrillation.

The action of magnesium on the heart has been explained as due to a depression of the cardiac nervous mechanism resulting in loss of tone (Matthews and Brooks, 1910), to a vagal effect, and to a direct effect on conduction (van Dellen and Miller, 1939). Smith, Winkler, and Hoff (1939) maintain that magnesium depresses the S-A, A-V, and intraventricular conduction. Pines *et al.* (1944) observed disturbances of A-V and intraventricular conduction from large doses of magnesium, but with smaller doses they were able to abolish ventricular fibrillation due to mercurial diuretics without affecting conduction. These findings suggest that magnesium depresses ectopic centres more than the normal conducting system, but that both are depressed by large enough doses.

To gain more information on the action of magnesium upon the conducting system, 10 cases with sinus rhythm were studied. In 5 of them the cardiogram was normal, and in 5 it showed T wave changes. In each case the limb leads were first recorded, and then usually lead II, immediately after the injection of 20 c.c. of a 20 per cent solution of magnesium sulphate, and two minutes later. Besides minor alterations in the rate in 4 cases, and the appearance of ventricular extrasystoles in 1, no changes were observed. These results are in agreement with those of Bernstein and Simkin (1939) who studied the effect of magnesium on the human

TABLE II

THE EFFECT OF MAGNESIUM ON EXTRASYSTOLIC ARRHYTHMIA

Case Number	Underlying heart disease	Cause of extrasystoles	Effect	Duration of effect
10 (Fig. 10)	Mitral stenosis	Digitalis	Decrease in voltage	Unknown
11 (Fig. 11)	Coronary thrombosis	Digitalis	Extrasystoles abolished	Lasting
16	Hypertension	Digitalis	Extrasystoles abolished	Ten minutes
17	Mitral stenosis	Digitalis	Change in shape of extrasystoles	Unknown
18	Mitral stenosis	Digitalis	Trigeminy	Few minutes
19	Mitral stenosis	Spontaneous	Nil	—
20	Nil	Spontaneous	Nil	—
21	Coronary thrombosis	Spontaneous	Nil	—
22	Mitral stenosis	Spontaneous	Nil	—

heart in normal cases and in those suffering from various forms of heart disease, and found that magnesium had no effect on the normal conductive system. The appearance of extrasystoles is a paradoxical effect which has also been noticed by others (Miller and van Dellen, 1941; Boyd and Scherf, 1943).

The intravenous administration of magnesium sulphate, in doses up to 20 c.c. of a 20 per cent solution, is a safe procedure and we have seen no untoward effect from it. It causes an unpleasant but transient feeling of intense heat due to a vasodilator action. Though several patients in this series died, the death was unrelated to magnesium sulphate; it was due in every case to the heart failure and condition of the heart that initiated the attack. The time interval between the giving of magnesium sulphate and death ranged from twenty hours to three months. The normal magnesium content of the serum is 2 to 3 mg. per 100 c.c. According to Goodman and Gilman (1943), the kidneys excrete magnesium so rapidly that the oral ingestion of magnesium salts results in only a slight rise in the serum magnesium. It is to be expected, therefore, that the serum magnesium, following a single intravenous injection of magnesium sulphate, will return very quickly to the original level. However, by continuous intravenous injection, Smith, Winkler, and Hoff (1939) were able to raise considerably the serum magnesium level. It is generally agreed that the excretion of magnesium is decreased, and correspondingly the serum magnesium increased in patients with renal failure (Hirschfelder and Haury, 1934; Brookfield, 1937; Haury, 1942; Winkler, Smith, and Hoff, 1942). Rubin and Rappaport (1941) warned against the possible danger of administering magnesium to anuric patients, and Hirschfelder and Haury (1934) concluded that hyper-magnesæmia was an important causal factor in many cases of so-called uræmic coma. One should be cautious, therefore, in giving magnesium to patients with renal failure.

SUMMARY AND CONCLUSIONS

The effect of intravenous injections of magnesium sulphate, 20 c.c. of a 20 per cent solution on the human electrocardiogram was studied in cases with sinus rhythm, paroxysmal tachycardia, extrasystolic arrhythmia, and auricular fibrillation.

It was found to have no significant effect on the normal conducting system, and it produced only minor changes in the normal cardiogram.

Out of 13 cases of paroxysmal tachycardia 9 were affected by magnesium sulphate; in 5 the effect was lasting, and in 4 only temporary, *i.e.* from three minutes to twenty-four hours. In 4 sinus rhythm was restored, in 1 the tachycardia was replaced by the original

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rhythm of auricular fibrillation. In the remaining 4 cases variable degrees of A-V block appeared. A dose of magnesium sulphate that has no appreciable effect on the normal conducting system, may depress impulse production in heterotopic centres. In increased myocardial irritability all parts of the conducting system may be depressed. The data presented justify the use of magnesium sulphate as a therapeutic agent in paroxysmal tachycardia. The intravenous administration of magnesium sulphate is a safe procedure, but its effect may be only temporary.

Extrasystoles caused by full digitalization were either completely abolished or altered by magnesium, while extrasystoles from other causes were not affected by it. Further investigation of the relationship between magnesium and digitalis is required.

Auricular fibrillation was not affected by magnesium.

The conclusions reached apply only to the human heart and to doses of magnesium sulphate specified. The results of animal experiments are not directly comparable.

I am indebted to Professor Hume for his helpful criticism and advice. I also wish to thank Dr. William Evans for his help and suggestions, Dr. I. E. McCracken, Medical Officer of Health, Newcastle-on-Tyne, and Dr. G. Hurrell, Medical Superintendent, Newcastle General Hospital, for facilities provided, and the Editors of this Journal for their help in reducing and rearranging the paper.

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RUPTURED CONGENITAL ANEURYSM OF THE POSTERIOR SINUS OF VALSALVA

BY

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Received April 6, 1946

The three sinuses of Valsalva are best described as right, left, and posterior, the last being the non-coronary sinus. An aneurysm may develop in relation to any of these, but the right sinus is the one most usually involved; the aneurysm then generally ruptures into the right ventricle. The posterior sinus is far less often implicated. It comes into close anatomical relationship to the right atrium, into which an aneurysm of this sinus is likely to rupture. Symptoms are unusual until shortly before death, which is often sudden, through perforation into the pericardium, pulmonary artery, right atrium, or ventricle. Those aneurysms that enlarge to the right may cause conduction disturbances by their proximity to the membranous portion of the interventricular septum.

Syphilis, ulcerative endocarditis, and atheroma are recognized causes of dilatation of the aortic sinuses, but the condition also occurs as a rare congenital anomaly. Abbott (1936) was able to collect records of 12 congenital cases; Micks (1940) described a case of congenital aneurysms of all three sinuses; while Hirschboeck (1942) reported an aneurysm of the right sinus, and Macleod (1944) one of the left. Brown (1939) mentioned two cases, in one of which the aneurysm arose from the right sinus and in the other from all three; in both these rupture occurred into the pericardium: he stated that in about half the congenital examples there was an additional defect of the bulbar septum just below the aneurysm.

Report of a Case

A housewife, aged 31, was admitted to Southmead Hospital on February 6, 1946, with symptoms and signs of heart failure.

At the age of 12, because she had had frequent fainting attacks, she was referred to Dr. Coombs at the Bristol Royal Infirmary. On examination he found that the apex beat was normal in position and extent. Pulsation was felt in the epigastrium. A loud musical systolic murmur was heard over the whole of the præcordium, maximal at the inner ends of the fourth and fifth spaces; it could also be heard between the left scapula and the spine. There was no cyanosis and no clubbing of the fingers. An X-ray did not show any cardiac enlargement, and the cardiogram was normal. There was no history to suggest rheumatic fever. Seen again a year later by Dr. Coombs, her condition was found to be unchanged. He considered the heart lesion to be congenital.

The patient herself was adamant that until two weeks before admission to hospital she was able to indulge in all normal activities without symptoms. She had passed through three labours without undue distress, and in none had she to take to her bed before the actual onset of labour pains. She had a vague recollection of having attended a cardiac clinic in youth but understood that she had outgrown her heart trouble.

Two weeks before admission, whilst sawing wood, she experienced a sudden, acute pain behind the lower part of the sternum, which radiated upwards into the throat and gave her a choking sensation. Because of the severity of the pain, and the repeated vomiting which soon accompanied it, she was forced to go to bed. The pain and vomiting continued for the following two days. She became increasingly short of breath and her legs and abdomen began to swell. Insomnia became troublesome.

On admission she was found to be dyspnœic. Her face was pale except for slight cyanosis in the cheeks and lips. There was engorgement of the cervical veins and those coursing over the upper part of the chest; these vessels showed pulsation. The apex beat was in the sixth space, two inches outside the mid-clavicular line. No thrills were felt. The heart was beating regularly at the rate of 120 a minute. All over the præcordium there was a rough, roaring systolic and a diastolic murmur. This was much louder over the tricuspid area than anywhere else, but it was also very loud over the

mitral area. Listening over the aortic area and along the left border of the sternum it was difficult to decide whether the murmurs heard were conducted from the tricuspid area or whether they were different in character and originating from the aortic valve. The blood pressure was 200 systolic, and 40 diastolic. There was dulness over both lung bases with diminished air entry and crepitations, more so on the right. There was a moderate amount of free fluid in the abdomen. The liver was enlarged three fingers' breadth below the costal margin, and could be felt to pulsate. The spleen was not palpable. There was gross œdema of the legs and the small of the back.

An antero-posterior X-ray of the chest, taken with a portable machine, showed gross dilatation of the heart and an opacity at the base of the right lung. A cardiogram revealed a regular A-V nodal rhythm at a rate of 120 a minute, and right ventricular preponderance (Fig. 1). The hæmoglobin

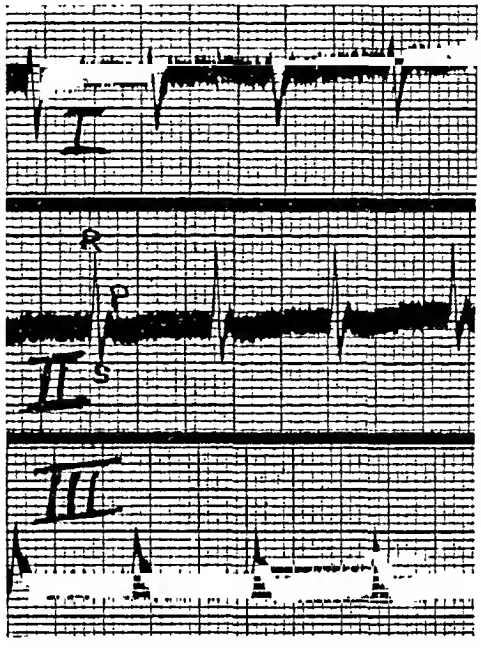

FIG. 1.—A-V nodal rhythm and right axis deviation. The heart is beating regularly at a rate of 120 a minute.

was 78 per cent (Haldane), the red blood corpuscles 4,400,000, and the white blood corpuscles 14,000 per cu. mm. Carotid and eyeball pressure had no effect on the cardiac rate. Treatment with restricted fluid and salt intake, full doses of digoxin, injections of mersalyl, and with sedatives produced no improvement, and had very little effect on the cardiac rate. The œdema and effusions into the serous cavities increased—the ascites had to be tapped. On February 25 her conjunctivæ were slightly jaundiced and urinary output was poor. She died rather suddenly at about noon on this day, shortly after addressing a remark to one of the nurses.

Post-mortem examination was performed 24 hours after death.

The body was well nourished, there was slight jaundice present and generalized venous engorgement with anasarca.

The abdominal and pleural cavities contained a large quantity of bile-stained fluid and the pericardial cavity also contained a slight excess of similar fluid.

The heart weighed 385 g. The right side was considerably dilated; the right atrium communicated with the left through a small aperture in the fossa ovalis; beneath this, lower down the interatrial septum and just above the septal cusp of the tricuspid valve, there was a saccular projection of thin membrane in the centre of which was a small hole 1 mm. in diameter; there was also a ragged perforation of this aneurysmal sac through a calcified part of its wall (Fig. 2). In the anterior margin of the septal cusp of the tricuspid valve there was a foramen 3 mm. in diameter leading directly into the left ventricle. The margins of the valve adjacent to this aperture were thickened and slightly discoloured: this was presumably due to the mechanical stress of the jet of blood entering from the left ventricle. The valve measured 13 cm. in circumference and appeared competent.

The right ventricular wall measured 7 mm. in thickness and the chamber appeared somewhat dilated. The pulmonary valve was normal.

The left atrium was not remarkable.

The mitral valve measured 9 mm. in circumference and was healthy.

The left ventricular wall measured 15 mm. in thickness and was not dilated or hypertrophied. Just below the point of fusion of the right and posterior cusps of the aortic valve there was a foramen opening through the anterior margin of the septal cusp of the tricuspid valve as described above.

The aortic valve was deformed; the right and posterior cusps were partially fused and there was a small fenestration in the free margin of the right cusp. The adjacent parts of these cusps were thickened (Fig. 3), but there was no generalized thickening as seen in rheumatic valvulitis. The valve

FIG. 2.—View of right atrium and tricuspid valve. The arrow points to the ruptured aneurysm with the orifice of the patent interventricular septum immediately below it. Note the roughening of the tricuspid leaflets. Magnification ×1·4.

FIG. 3.—Aortic valve. The sinuses of Valsalva enumerated from left to right are: right, posterior, and left. The interventricular septal defect lies immediately below the fused right and posterior cusps. Magnification ×1·4.

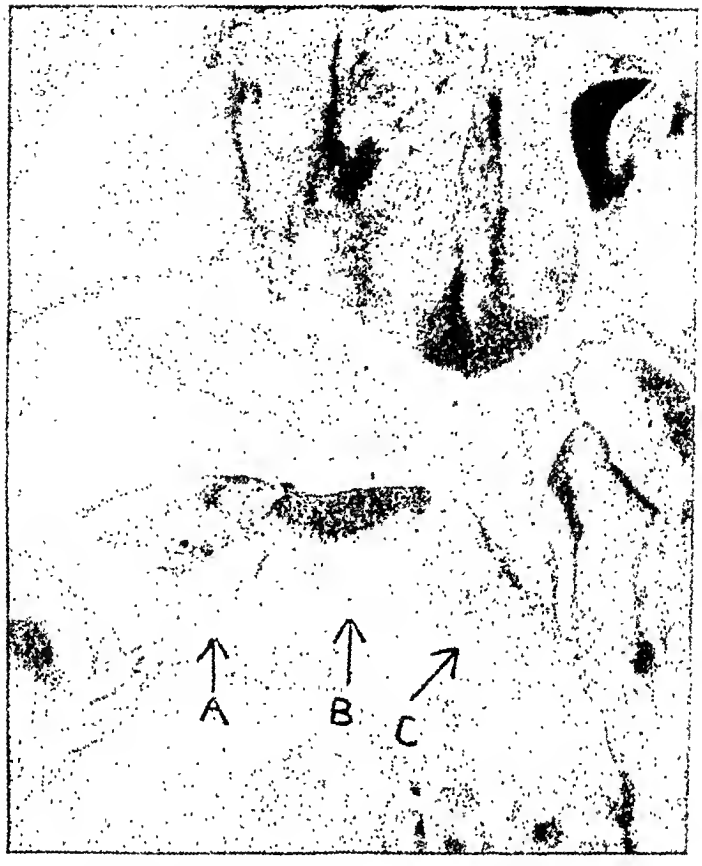

FIG. 4.—Sinuses of Valsalva as viewed from above.
(A) Aneurysm of right sinus.
(B) Aneurysm of posterior sinus leading into right atrium.
(C) Normal left sinus. Magnification ×1·4.

measured 6 cm. in circumference (normal 8 cm.). The right sinus of Valsalva was considerably dilated and stretched back into the muscle of the interventricular septum. The floor of the posterior sinus of Valsalva consisted of an aneurysmal sac leading into the right atrium (Fig. 4). The left sinus of Valsalva was normal.

There was no evidence of any rheumatic or infective endocarditis, past or present.

There was slight atheroma of the abdominal aorta. The left renal vein passed behind the aorta.

Both lungs were very congested and moderately œdematous.

The spleen was not enlarged and appeared normal on section.

The liver showed intense venous congestion, and histologically there was considerable central necrosis, sufficient to account for the jaundice. There was no evidence of chronic congestion.

The gall-bladder and bile ducts were healthy and patent.

Both kidneys showed venous congestion. There was a double ureter on the left side.

Anatomical diagnosis. Congenital aneurysms of the right and posterior aortic sinuses of Valsalva with rupture of the posterior sinus into the right atrium. Patent interventricular septum. Fusion of the right and posterior cusps of the aortic valve. Right ventricular hypertrophy. Congestive cardiac failure with terminal hepatic jaundice.

DISCUSSION

Some writers (Goehring, 1920) have considered a deformity of the aortic valve cusps similar to ours to be a bicuspid valve, but this is not admissible as the adjacent raphé between the right and posterior cusps was still present.

Histological examination of the liver showed that the venous congestion was of recent origin, and it seems probable therefore that it dated approximately from the time of rupture of the aneurysm.

The sudden onset with pain, shock, and vomiting, signs of aortic insufficiency, and the rapid development of heart failure in a previously healthy subject characterize most of the

detailed reports of this condition. This clinical picture may also be produced by rupture of an aortic valve cusp and sometimes by a dissecting aneurysm involving the aortic ring. As in coronary occlusion, leucocytosis and even elevation of the temperature may be found. In both the case reported by Micks (1940) and in that by Duras (1944) there was heart block. Other conduction disturbances have been recorded.

In many of the reports the clinical details are scanty, because of the rapidity with which death follows rupture. Both Hirschboeck (1942) and Macleod (1944) reported rupture of an aortic sinus into the right atrium; in both these cases and in our own the clinical pictures were very similar.

In the case reported by Hirschboeck the aneurysm arose from the right sinus of Valsalva. There was a systolic thrill over the apex, and a harsh systolic murmur was audible at the lower end of the sternum and in the epigastrium. On admission the blood pressure was 300/0 and the heart rate was 140 a minute. Liver dulness extended about two fingers' breadth below the costal margin. The leucocytes were counted on two occasions—on the first occasion the count was 11,400 per cu. mm. and on the second 18,800 per cu. mm. The temperature fluctuated from normal to 103° F. Five days after admission a diastolic murmur was heard at the base and along the left border of the sternum. A diagnosis of aortic and tricuspid insufficiency caused by endocarditis of undetermined origin was made. Right axis deviation had been found in the cardiogram and in view of the extreme hypertension this was considered to be unusual. Macleod described the onset of symptoms in his patient as sudden with abdominal pain, vomiting, and breathlessness. A harsh systolic murmur was heard all over the heart, loudest in the aortic area, and at the right border of the sternum there was a soft diastolic murmur. There was a water-hammer pulse, and engorgement and pulsation of the veins of the neck. A cardiogram showed auricular fibrillation. Necropsy, five weeks after onset, revealed an aneurysm of the left sinus of Valsalva, which had ruptured into the right atrium.

In our case the murmur noted in childhood was no doubt due to the communication between the left ventricle and the right atrium. This lesion does not appear to have caused any gross functional disturbance.

The sudden onset of symptoms can best be explained by rupture of the posterior sinus of Valsalva into the right atrium. The loading of the right atrium with blood from the aorta during auricular diastole explains the venous congestion and the pulsation in the veins of the neck and liver, while the same leak of blood out of the aorta accounts for the marked water-hammer pulse. The roaring systolic and diastolic murmur, heard best over the tricuspid area, is also accounted for by the anatomical findings. From a functional point of view a similar disturbance of cardiac dynamics would result from a combination of tricuspid and aortic regurgitation, and this was the diagnosis during life.

The A-V nodal rhythm was probably due to irritation of the A-V node by the aneurysm. The right axis deviation is readily understood, and as pointed out by Hirschboeck (1942), may have some diagnostic value when coupled with a water-hammer pulse. If the existence of such a lesion is borne in mind diagnosis after rupture is sometimes feasible.

Our thanks are due to Dr. Phillips, Medical Superintendent, Southmead Hospital, Bristol, for permission to publish this case; and to Professors Perry and Hewer for helpful criticism. We should also like to thank Mr. S. A. Edwards for the photographic reproductions.

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HEALED DISSECTING ANEURYSM

BY

MAURICE CASSIDY AND JOHN PINNIGER

From St. Thomas's Hospital

Received February 2, 1946

Since Shennan (1934) published his well-known report on 300 cases of dissecting aneurysm the literature of this condition has become extensive, and Sailer (1942) stated that there were then some 500 published cases, of which 33 had been diagnosed before death. There is general agreement that in some 80 per cent of these cases death occurs within a few hours of an acute onset, and that most of those patients who survive the accident of dissection are cardiac cripples who usually die of internal hæmorrhage or of cardiac failure within a year or two. There are, however, exceptions, such as Hall's (1926) patient, a boy aged 17, in whom the dissection occurred after a race, with such good recovery that he led a strenuous athletic life for 15 years. The survival record seems to be held by Graham's (1886) patient, who lived for 30 years after the dissection.

There is general agreement, too, as to the diagnostic criteria of the acute phase of the dissection. These have been well summarized by East (1939), who at the same time reports a personal case, diagnosed before death, of a woman, aged 43, who survived 5 years after the onset, despite a pressure of 300/150 during this period. That the healed dissection may be diagnostically obscure is pointed out by Gouley and Anderson (1940), who describe six patients in whom the onset was insidious and the clinical picture was that of cardiovascular syphilis. Pain was absent in four, inconspicuous in one, and occurred only intermittently for three weeks before death in one. All exhibited cardiac decompensation for periods varying between two months and four years. They all had big hearts, aortic regurgitation, and a dilated aorta radiographically: the Wassermann reaction was positive in one case only.

Others who have described aortic regurgitation with normal cusps in dissecting aneurysms are Resnick and Keefer (1925), Borger (1906), and Letulle (1905).

The case we now publish was, like those of Gouley and Anderson, diagnosed as syphilitic aortic reflux and aneurysm, though the possibility of a dissecting aneurysm was considered. The case is also of interest as illustrating the remarkable capacity for effort on the part of this victim of a healed dissection.

A Dutch engineer, aged 42, was first seen on March 19, 1942. He had gonorrhœa in 1921; his Wassermann reaction was then negative. In 1936, when aged 36, he played a long set of singles at lawn tennis in Holland and became so abnormally distressed that he had to stop. A week later, at 9 p.m., he was seized with very severe epigastric pain, which radiated to the angles of the scapulæ, more severely on the right side. He said that for two or three nights he was walking about in agony, and that morphia had to be injected, and that the pulse was said to have been very irregular : renal colic was diagnosed. He stayed at home for a fortnight, and subsequently resumed work, after which he noticed a tendency to dyspnœa and palpitation on vigorous exercise. In February 1937 he was investigated in a Dutch hospital; the aorta was " enlarged " and though the " blood test " was negative, he was given a course of intravenous arsenic. After this he was well enough to swim, and to play tennis, but not with his former vigour.

In 1940 he escaped from Holland on foot with his wife and children, carrying much baggage. He was able to swim and play tennis after his arrival in England that summer.

During January and February 1942 he became increasingly dyspnœic on exertion, and there was paroxysmal dyspnœa at rest. When examined on March 19, 1942, he was a

well-built man, not dyspnœic at rest, and presenting no evidence of congestive failure. Pulsation was seen and felt to the right of the sternum, where there was a diastolic shock. The presence of dilated venules along the line of diaphragmatic attachment suggested early vena azygos obstruction. The pulse was 92, with frequent premature beats; the blood pressure 140/60; and the arteries not unduly thick. On auscultation, a loud diastolic murmur was heard at the base and down the left sternal edge; the murmur was louder to the right than to the left of the sternum. No tracheal tug was felt. The knee jerks were brisk, and the pupils a little sluggish to light and not quite circular. On X-ray screening, the whole thoracic aorta was diffusely dilated. There was a considerable degree of left ventricular enlargement (Fig. 1), and the trachea was displaced to the right. His electrocardiogram showed numerous right ventricular premature beats, but was otherwise normal (Fig. 2, A).

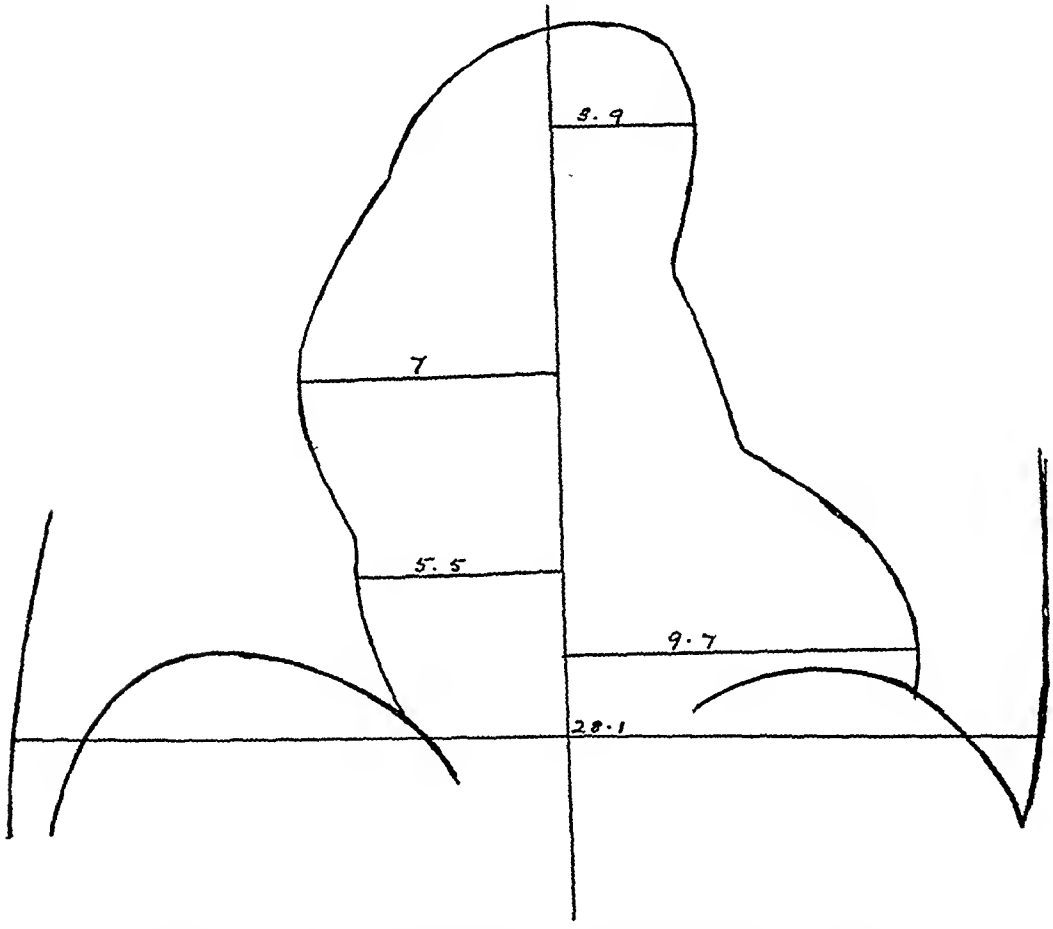
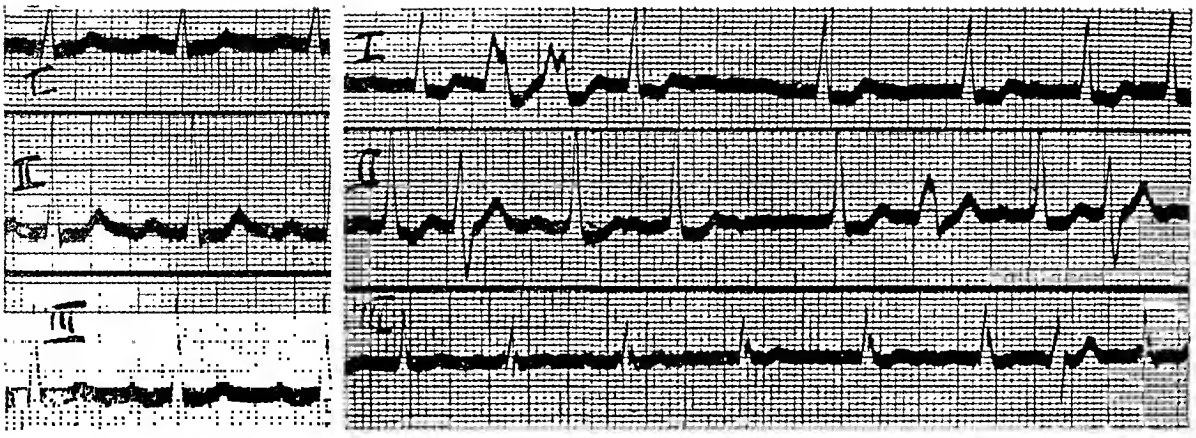


FIG. 1.—Orthodiagram on 25/5/42, showing left ventricular enlargement and dilatation of the aorta.

The diagnosis was aortic aneurysm, with aortic regurgitation. In view of the acute onset after violent physical effort, the possibility of either a ruptured valve or of a dissecting aneurysm was discussed. The latter diagnosis was considered to be improbable, because, apart from the onset, the clinical picture was typically that of a non-dissecting thoracic aneurysm. Moreover the radial and femoral pulses were equal, and it was thought that the combination of a dissecting aneurysm with free aortic regurgitation would hardly allow such a degree of physical activity as the patient had proved himself to be capable of. In spite of the fact that his Wassermann reaction was negative he was treated with mercury and iodide, and subsequently with stovarsol orally. When seen on May 25, 1942, he was working at his office full time, dyspnœic only on hills, and sleeping well with only one pillow. Dr. Anwyl Davies thought that in spite of the negative W.R. the condition was almost certainly syphilitic and advised further treatment with mercury and iodide.

In January 1944 he was still hard at work and almost symptomless, except for what



A B

FIG. 2.—Electrocardiograms. (A) Normal rhythm on 24/1/44. (B) Auricular fibrillation with ectopic beats on 21/5/44.

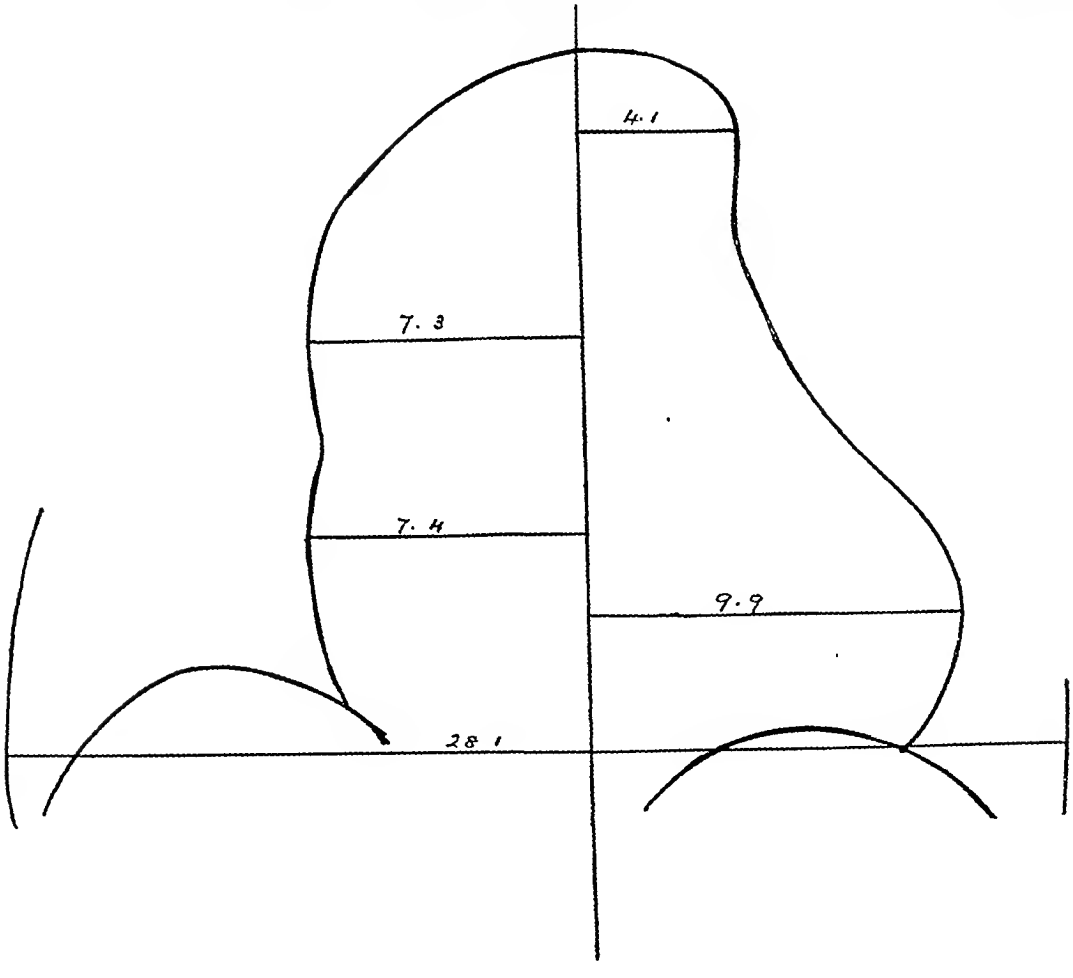


FIG. 3.—Orthodiagram taken on 9/1/45, showing further enlargement.

sounded like a paroxysm of auricular fibrillation during influenza a month previously. He had spent some months in Sweden, flying there and back under war-time conditions. Radiographically both heart and aorta were a little bigger. The electrocardiogram was unchanged.

In April 1944 there were further paroxysms of auricular fibrillation, lasting about two hours, and his condition had deteriorated when seen on May 21, 1944. Fibrillation had now become permanent, with multiple ventricular ectopic beats (Fig. 2, B). He was strongly advised not to follow the army of occupation into Holland, but felt that his knowledge of

the Dutch canals and their pumping stations was so unique that he insisted on going. He went by air to Brussels in September 1944. On his return he was able to work in his office only two or three days a week. He was increasingly dyspnœic on slight exertion, but his ventricular rate was easily controlled by a small dose of digitalis, and there was no congestive failure. In January 1945 an orthodiagram showed some further enlargement to the right (Fig. 3). Subsequently his condition deteriorated rapidly, and on March 4, 1945, he was admitted to St. Thomas's Hospital on account of increasing paroxysmal dyspnœa without evidence of congestive failure. On March 17, at 9.30 p.m., there was a sudden onset of sternal pain with severe dyspnœa, rapid pulse, sweating, and pulmonary œdema. He improved under morphia, but died within a few minutes at 10.30 a.m. on March 18.

Autopsy Report

The body was that of a well-nourished adult male.

Heart. A moderate excess of straw-coloured fluid was present in the pericardial sac. The heart was greatly enlarged, both sides showing the increase, but particularly the left. On section, the left ventricle showed hypertrophy, the thickness of its wall varying between 1·5 and 2·0 cm. Its cavity was dilated, the maximal internal diameters being approximately 7 cm. horizontally and 9 cm. in the superior-inferior direction. The right ventricle showed these changes to a corresponding degree, the thickness of its wall varying between 0·6 and 1·0 cm., and its internal diameters being both approximately 8 cm. The ventricular muscle appeared homogeneous and of normal consistency. The left auricle contained a thrombus in its appendix of approximately 1·5 cm. in diameter.

The tricuspid and pulmonary valves were normal. There was slight thickening of the edge of the posterior cusp of the aortic valve, and atheroma of the aortic cusp of the mitral valve. The aortic ring appeared dilated, its diameter being about 3 cm. The site of the intra-pericardial part of the aorta was occupied by a soft spherical mass having maximum diameter of 7·5 cm. (Fig. 4). The swelling lay superior to the right ventricle and anterior to

Fig. 4.—Heart and intra-pericardial aneurysm (anterior aspect). (A) Aneurysm.

the right auricle, compressing the latter posteriorly. Its surface was smooth, shiny, and for the most part of pale, blue-white colour. The mass was not adherent to any of the surrounding cardiac tissue except at the line of junction.

The coronary arteries were normal except for very slight patchy atheroma.

Aorta. On section, a horizontal rent in the intima was seen, extending from above the middle of the left posterior cusp round the left side across the anterior surface to the right lateral aspect, terminating just posterior to the union of the anterior cusp with the right posterior one. The maximal width of the rent was 2·5 cm.; its length was approximately 8 cm. The edge of the rent above the left posterior cusp was formed by free intima, which extended for about 3 cm. along its length. Here the floor was recently formed blood clot, part of the surface of that filling the intra-pericardial aneurysmal dilatation (Fig. 5). For the rest of the rent, the intima was bound by adhesions in an irregular manner to the media,

FIG. 5.—The same after opening. (A) Left ventricle. (B) Aorta. (C) Aperture into aneurysmal cavity showing surface of blood clot within.

FIG. 6.—More detailed picture of the split. (A) Left ventricle. (B) Rent in aorta, showing adhesion of split intima to underlying media.

which in this area also formed the floor (Fig. 6). The maximal width of the intimal tear was at the site of the visible portion of the blood clot and the adjacent area of the medial floor.

At the line of contact of the above-mentioned blood clot and medial floor, i.e. approximately superior to the junction of the anterior and left posterior cusps, there was free space which communicated superiorly and slightly to the right with a dissection in the posterior part of the ascending aorta. That part of the vessel immediately inferior to this free space showed slight saccular dilatation and gross irregularity of surface, much of which was due to localized atheroma.

It was apparent that the free space above mentioned formed the path of flow for the blood into the dissected false passage, and the small saccular dilatation and roughening of the aortic surface below was brought about by the impinging of the blood here on its passage through. The aneurysmal dilatation into the pericardium and the rent with a free intimal edge indicated a much more recent change.

The dissection, which initially lay posterior, tracked slightly to the left as it progressed upwards. The aneurysm thus formed posterior, inferior and right lateral relationships. The left lateral relationship was formed by the left pulmonary artery. The diameter of the dissection was here approximately 3 cm.

In the region of the arch of the aorta the false passage lay posterior and slightly inferior. There was only very small penetration upwards round the beginning of the innominate, left common carotid and subclavian arteries, reaching a maximum of 0·5 cm. These vessels thus formed the most superior border of the false passage (Fig. 7). As the aorta curved down-

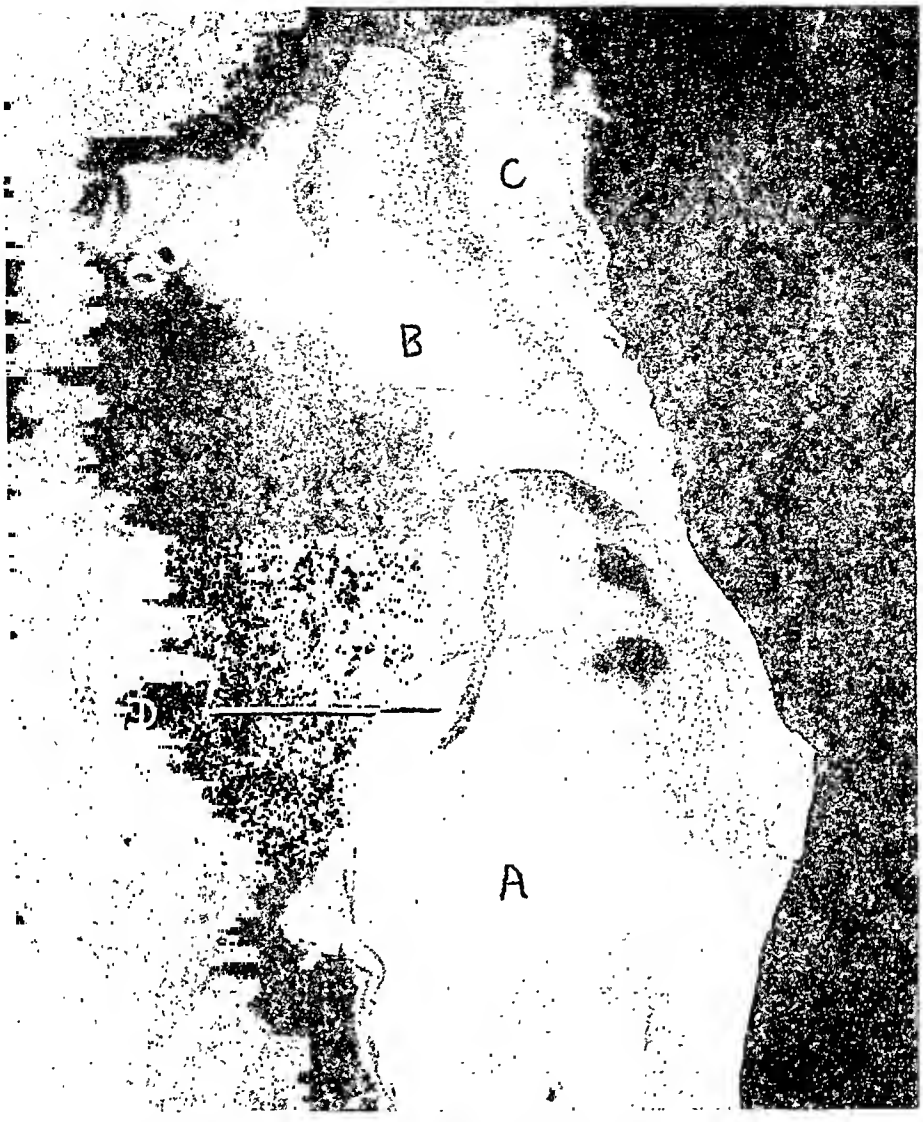


FIG. 7.—A view of the aorta further on. (A) Descending thoracic aorta. (B) Innominate artery. (C) Left common carotid artery. (D) False passage.

wards the false passage changed its posterior and inferior relationships to a posterior and slightly right lateral one, but when the diaphragm was reached it lay exactly posterior. At the bifurcation of the abdominal aorta the false passage lay right lateral (Fig. 8). Here the true aorta appeared continuous with the left common iliac artery, whereas the false passage descended down the right one for approximately 4·5 cm., 0·7 cm. above the division into the internal and external iliac branches. The site where the false joined the true arterial channel was clear cut. The former lay at first right lateral and then anterior to the first part of the true right common iliac channel, with the result that the free edge of union lay posterior to the former and anterior to the latter. The opening of the true right common iliac artery into the aorta had become displaced as a result of the dissection, appearing as a slit-like branch of the aorta where it became continuous with the left common iliac artery.

The false passage showed atheroma with ulceration and calcification on the wall not shared with the true passage, the change being most severe in the right common iliac artery 1·5 cm. up from the site of junction with the true iliac artery. It extended, however, also upwards to a point approximately 4 cm. from the bifurcation. There was no

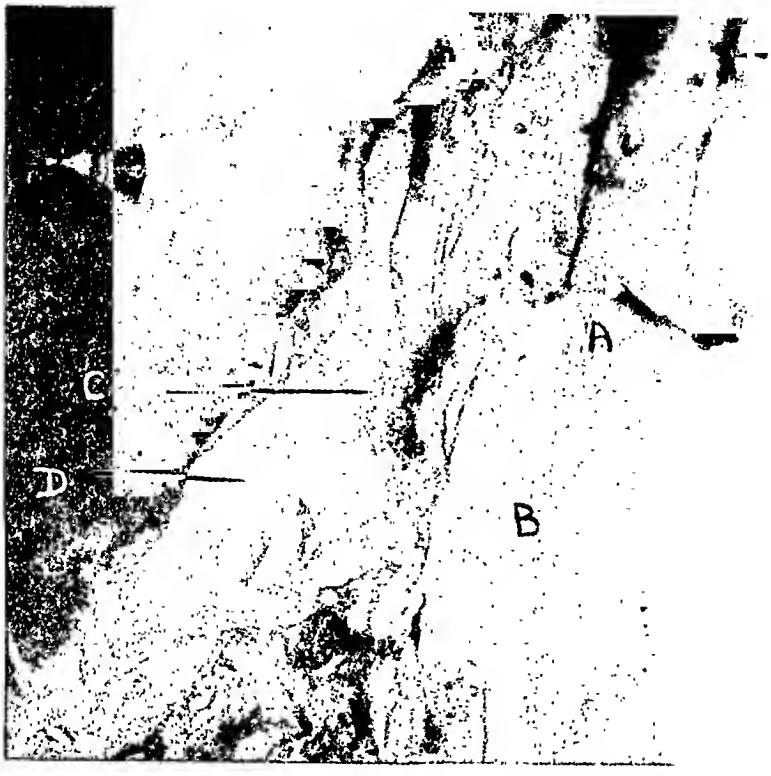


FIG. 8.—Bifurcation of the abdominal aorta. (A) The distal end of the aorta. (B) Left common iliac artery. (C) Atheromatous plaque in false passage. (D) Line of union of false passage with the true right common iliac artery.

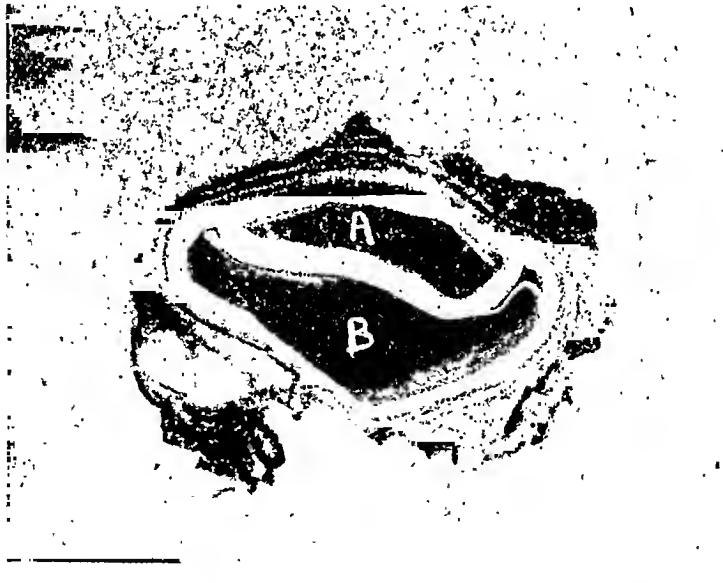


FIG. 9.—Cross-section of aorta at the level of the diaphragm. (A) True passage. (B) False passage.

change to a similar degree on the common wall in the corresponding places. The true aorta was also moderately atheromatous in all its extent. The posterior wall of the false passage showed in addition great unevenness of surface, raised white areas standing out from depressed more grey-white areas. There was also considerable wrinkling of the surface, particularly in a longitudinal direction.

Cross-section of the two channels at the level of the diaphragm revealed the internal diameter of the aorta when compressed to be 2 cm. and that of the false passage 3 cm. Thus there was a tendency for the latter to flank the former on its lateral aspects (Fig. 9).

The thickness of the true aorta varied from 0·15 cm. to 0·2 cm. The wall common with the false passage was only slightly less thick than the unsplit portion. The posterior wall of the false passage measured 0·10 cm. The cross-section of the common wall was clearly made up of three layers, a central yellow portion and slightly thicker light grey portions on either side. On the anterior aspect of the true passage the yellow layer became compressed and the inner light grey layer was proportionately more thick. The rest of the wall of the false passage was composed of light grey tissue only. The outer wall of the whole was covered by a very thin layer of softer pinkish-grey tissue.

The weight of the heart together with the intra-pericardial aneurysm and its contents was 1190 g.

Branches of aorta. The intercostal artery openings were patent in the true aorta, and some were linked with corresponding openings in the false passage by thin strands of fibrous tissue. The cœliac, superior mesenteric, inferior mesenteric, left renal, and left testicular arteries opened direct into the true channel. The right renal and right testicular joined the false channel, corresponding apertures being present also in the common wall. All the lumbar branches of both sides opened into the false passage. The corresponding apertures in the true passage were patent, and some of these, like the corresponding intercostal vessels, were linked by fibrous strands to the false passage openings. The middle sacral artery was not involved in the dissection and therefore opened into the true passage immediately above the bifurcation.

Respiratory system. There was a large excess of straw-coloured fluid in the left pleural cavity. Firm adhesions were present between the parietal and visceral pleuræ on the right side, especially in the basal region. A small excess of pleural fluid was present in this cavity also. The trachea and main bronchi were full of frothy straw-coloured fluid. The lungs (right—1021 g.; left—794 g.) were extremely œdematous, but apart from patchy basal collapse, slight congestion, and emphysema they showed no further macroscopic abnormality.

The *liver* (2168 g.) showed moderate nutmeg change.

The *spleen* (298 g.) was firm, cut crisply, the cut surface being of deep purple colour.

The *left kidney* (383 g.) was congested.

The *right kidney* (326 g.), in addition to this change, contained an infarct in its upper half. The surface area involved was approximately 2 cm. square, having an irregular contour. The central part was light yellow and immediately surrounding it there was a zone of congestion. On section the infarct was shown to be wedge-shaped, the apex reaching the rim of the pelvis.

The remaining *abdominal organs* showed congestion.

There was a cortical adenoma in the *left adrenal*, 1·2 cm. in diameter.

The head was not opened. There was no macroscopic abnormality of mouth, larynx, pharynx, and thyroid.

Histology

Aorta. Sections were cut of the vessel (1) at the site of the rent and (2) just superior to the diaphragm. They were stained with hæmatoxylin and eosin, Van Gieson's stain, a modification of Weigert's elastic stain, and with Scharlach R for fat.

(1) The section was taken longitudinally through the aortic wall to include an area of the rent where the media formed the floor, and where the pulmonary artery was contiguous with the vessel. The media of the aorta here showed advanced degeneration. There was extensive fibrous replacement, diffuse mucoid degeneration and a few patches of necrosis. In one or two places the mucoid change had led to the formation of small lakes in the medial tissue. No fatty degeneration was demonstrated. The intima was a little atheromatous and the adventitial coat had undergone hyaline fibrosis.

(2) The split had taken place in the media approximately at the junction of the inner two-thirds and outer third (Fig. 10). The internal elastic lamina and the stripe of the true channel were not easily seen throughout the whole circumference of the vessel. The intima

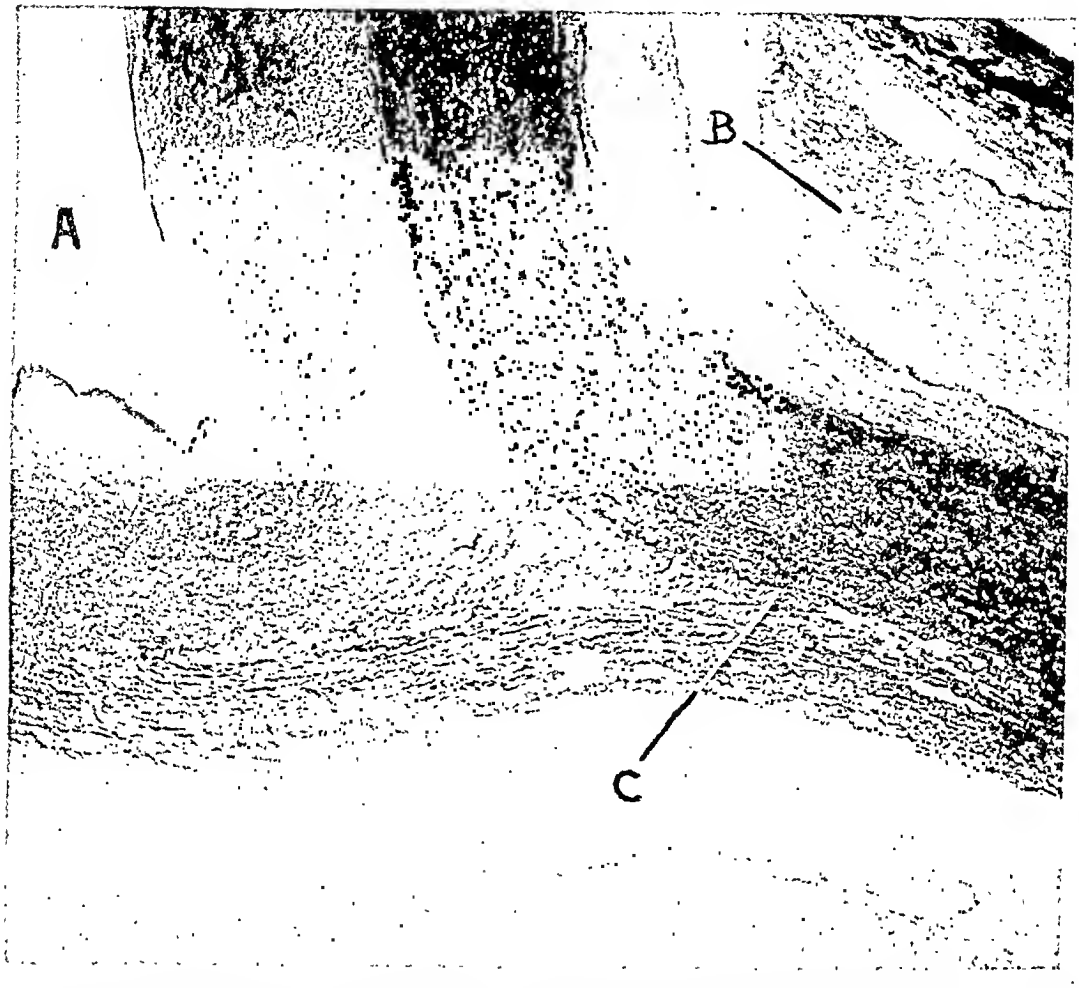


FIG. 10.—Photomicrograph of aorta at the level of the diaphragm (modified Wiegert's stain). (A) Lumen of false passage. (B) Intima of true passage. (C) The site of split in the media.

showed marked hyperplasia for about a third of its circumference, i.e. for the extent of nearly the whole of the wall not shared with the false channel. This hyperplasia was most marked between the internal elastic lamina and the stripe; the hyperplastic tissue showed also a hyaline degeneration. In the area of intima contiguous to the split in the media there were some fair-sized capillary blood vessels.

The false channel partly overlapped the true channel. The wall showed a variable thickness. The wall common with the true passage consisting of approximately two-thirds of the original media was thicker than that elsewhere. The thinnest portion was that diametrically opposite this common wall where there were only a very few elastic fibres. The media showed a progressive diminution in thickness between these two points. Under low power, in the section stained with hæmatoxylin and eosin, the false passage showed an inner layer of pale staining tissue, an intermediate zone staining light pink, the original media giving a deep pink, and lastly the outer adventitial zone. It appeared thus that a new " intima " had been formed. The elastic stain section showed that in both the inner and intermediate zones there was still considerable elastic tissue, the density of this becoming less as the lumen was approached, this diminishing content of elastic tissue accounting for the progressive lightening of the stain in the hæmatoxylin and eosin section. In both these zones the elastic tissue was very degenerate, contrasting sharply with that in the normal media. As a result of the high content of elastic in the new " intima " the inner surface of this false tube showed fine corrugation. Its surface was covered by a single layer of flattened endothelium. At that angle formed by the medial split which was not associated with intimal hyperplasia in the true passage there was a small valve-like projection from the " intimal " surface of the false passage. This consisted of a central core of dense elastic surrounded by a rim of less dense and degenerate elastic.

The adventitia surrounding the whole vessel was comparatively normal. A few elastic fibres were present. Collagen was a little more dense outside the free wall of the false passage where the elastic media was thinnest. The small vascular channels were dilated and full of blood and there had been hæmorrhage into the surrounding tissue. Round one of these vessels there was an accumulation of small round cells.

In summary, the histological picture confirmed the clinical conclusion that dissection down the aorta had occurred a considerable time before death. The period of active repair had passed and endothelium had formed on the surface of the false passage. Further, the appearance of atheromatous degeneration with surface ulceration and calcification in those parts of the false passage not shared with the true passage, without any corresponding change in the wall common with the true passage, is added evidence that the dissection was of old standing.

Kidneys. Both congested. Right kidney, four recently infarcted areas: an artery in relation to the largest of these contained a small recent thrombus. The capsule and the perirenal fatty connective tissue overlying the infarcted areas showed organizing chronic inflammatory granulation tissue. Adrenal congested with cortical adenoma.

Liver and spleen. Venous congestion, and slight fatty degeneration of liver.

Lungs. Slight congestion. Œdema. Emphysema.

Summary and Conclusions

A case of healed aneurysmal dissection of the aorta, of nine years' duration, is described. For some years the patient was able to live a very strenuous life, till symptoms of left ventricular failure appeared, the diagnosis then being syphilitic aneurysm with aortic regurgitation.

The autopsy findings are reported in detail.

There can be little doubt that the original dissection occurred in 1936, nine years before death. The diagnosis at this time was renal colic, and it is interesting to find that the right renal artery arose from the false channel. Renal colic and hæmaturia have been described in reports of acute dissections, which sometimes involve one or both renal arteries.

The histological appearances of the aorta at the site of the intimal tear conform with those of idiopathic cystic medio-necrosis of the aorta (Erdheim, 1929; Moritz, 1932; Roberts, 1939; and Davies, 1941). It is not unreasonable to assume that these changes were present to a degree at the time of the original accident.

Our thanks are due to Mr. A. E. Clark, for his assistance with the photographs, and to Dr. R. W. L. Todd, who referred the patient to us.

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EDITORIAL NOTE ON ANOTHER HEALED CASE

With the approval of the authors the notes of another healed case are added. Dr. A. G. Gibson has given me details of a woman where recovery was complete but unluckily she had no relatives from whom a history of the original illness could be obtained. She died from a cerebellar hæmorrhage and all that was known was that she had worked as a domestic servant for the last six years of her life without any serious illnesses or disability.

The whole aorta consisted of a double tube from just below the origin of the left subclavian artery to the left iliac artery. The figure (Fig. 11) shows the opening of the true aorta.

Autopsy by Dr. A. G. Gibson

A well-nourished woman, aged 46.

Heart. Hypertrophied. Sclerotic thickening of one aortic valve cusp. Atheroma at base of aorta and anterior leaflet of mitral. Both ventricles hypertrophied. No pulmonary embolism. Coronaries thickened but patent.

Thyroid. Large degenerating cyst in upper pole of l. lobe.

Aorta. Beginning from the descending part of the arch just beyond the left subclavian artery was another tube attached to the inner and posterior wall, heading down through the abdominal aorta to end in the left iliac artery one inch from its origin from the aorta. There was a wide opening at its origin in the aorta.

Lungs. Both collapsed.

Abdominal viscera. Normal except for some congestion.

Kidneys. Left: small, congested, slightly granular; arteriosclerotic scars. Right: diminished cortex; as left. Suprarenals. Both hypertrophied cortex.

Brain. Bleeding into both lateral ventricles (liquid). Clotted blood in the 3rd ventricle, in the iter and the 4th ventricle. Massive hæmorrhage in the middle part of the cerebellum which had reached the surface of the r. lobe. Some bleeding into anterior r. middle and posterior fossæ. Right sphenoidal sinus double. Lower one thickened mucosa and slight pus. Maxillary antra nil.

FIG. 11.—Photograph of the aorta, showing the opening of the true aorta and a healed dissecting aneurysm.

MAURICE CAMPBELL

SILENT DISSECTION OF THE AORTA

BY

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From the Cardiological Department of the Royal Free Hospital

Received March 27, 1946

Dissecting aneurysm of the aorta has been known as a pathological entity for over a century (Maunoir, 1802); it was first diagnosed during life by Swaine (1856), and a full account of its clinical and pathological features was given by Peacock in 1863. Even so, until recently only thirteen accurate ante-mortem diagnoses had been reported (Glendy *et al.*, 1937). Failure to diagnose the condition has been mainly due to its relative infrequency and to consequent lack of clinical suspicion. In a large series, Shennan (1934) reported one dissecting aneurysm in every 175 autopsies; Reich (1944) reported the average incidence as one in 380 autopsies, while in our own hospital it has been found only twice in the 900 autopsies performed during the last six years. In the last decade, however, clinicians have become increasingly aware of the condition and a further 84 cases, accurately diagnosed during life, have been reported.

Although about 80 per cent of patients die within the first few days of dissection, accurate diagnosis is important because, in a small number, life and moderate health may be sustained for some years with appropriate supervision. The classical picture of dissecting aneurysm has been repeatedly described (Peacock, 1863; Gager, 1926; and White *et al.*, 1935). The sudden onset of severe and prostrating pain, widely distributed throughout the body, together with evidence of interference with the blood flow in vessels arising from the diseased aorta, the appearance of an aortic diastolic murmur and a history of long-standing hypertension, form a syndrome which is not difficult to recognize once its significance is appreciated. Rare cases had, however, been reported where pain was absent and yet a recent or healed dissection was found at autopsy. These silent dissections are generally limited in extent, and it is not surprising that, in the absence of the characteristic pain, they are rarely suspected during life.

We report the following case because we have evidence of a silent dissection of the aorta. It was possible to make the diagnosis during life because the patient suffered a second attack characterized by the classical features of dissecting aneurysm. We believe this case to be of interest because the patient survived a second dissection of his aorta for over eighteen months, and because his illness was complicated by paroxysmal auricular flutter.

Case Report

The patient, a cinema agent of 56, was first seen by us in October 1942. He had been breathless on exertion for two years, but recently had grown so much worse that a walk of only a few yards would cause him severe distress. During these two years he had had attacks of palpitation ; these might come on at any time and usually lasted a few hours. On questioning, he admitted to occasional substernal discomfort but at no time had he had any severe præcordial pain. Four years earlier he had been treated by rest in bed for obesity and hypertension.

Examination showed an obese Hebrew with cyanosis; he was so breathless that the slightest exertion caused him real distress. The pulse rate was 140 a minute, the rhythm irregular, and the blood pressure 180/130 in both arms. The heart was enlarged; there was a triple rhythm and a harsh systolic murmur at the apex and a ringing second sound in the aortic area. There was some congestion at the right lung base.

X-ray examination of the chest revealed an enlarged heart and an enormously dilated and

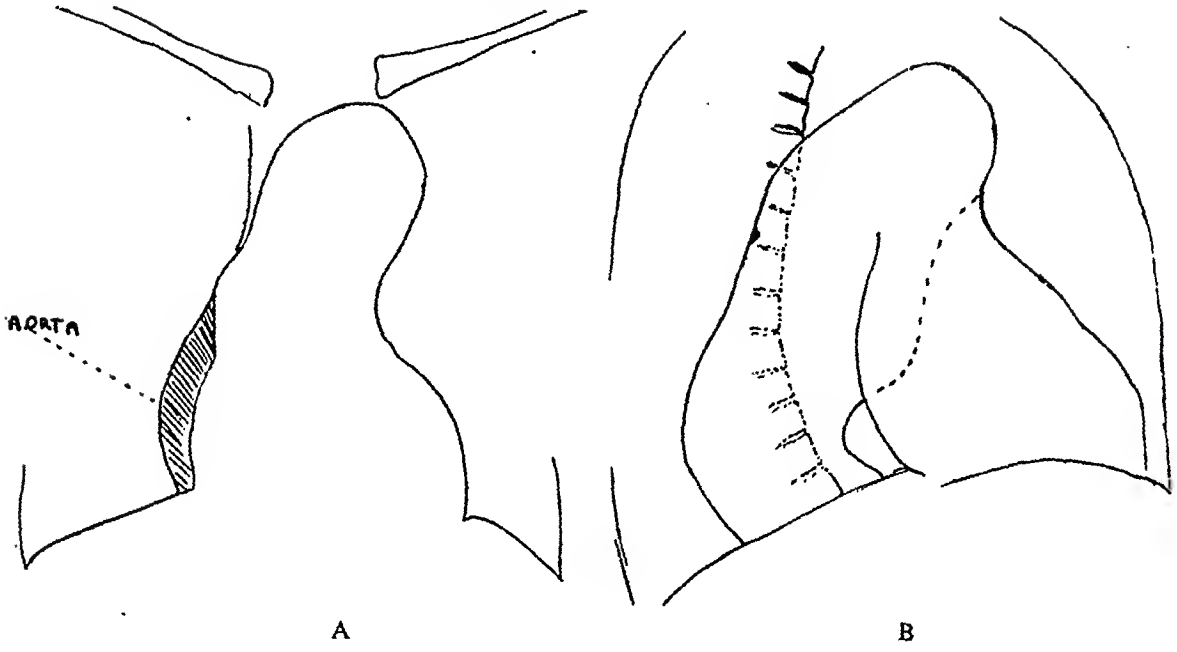


FIG. 1.—Orthodiagrams. 16/10/42.
(A) Showing dilated and tortuous aorta.
(B) Right (I) oblique position. The extent of the aortic enlargement can be clearly seen.

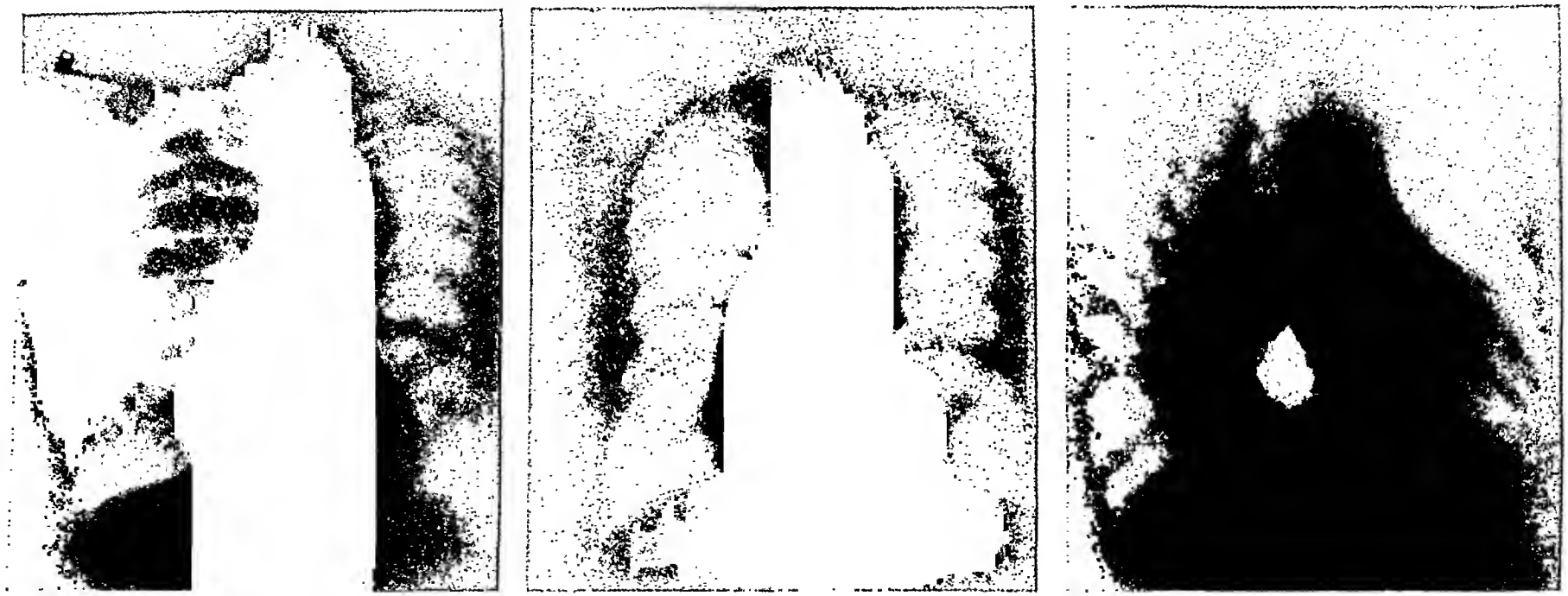
tortuous aorta (Fig. 1 and 2, A). The latter was seen more clearly on screening, when the lower thoracic aorta could be recognized lying behind and extending to the right of the right border of the heart (Fig. 1). The cardiogram showed irregular 2 : 1 and 3 : 1 auricular flutter (Fig. 3). The Wassermann and Kahn reactions were negative.

He was admitted to hospital and given digoxin, 0·25 mg. six-hourly by mouth. Normal rhythm was restored on the fourth day of treatment and there was sinus rhythm with depression of S–T II and III, compatible with digitalis therapy (Fig. 3, B). A diagnosis of atherosclerosis of the aorta associated with long-standing hypertension was made.

Thereafter he improved rapidly; the pulmonary congestion cleared and, when discharged three weeks later, he was no longer breathless when up and about. On discharge, quinidine sulphate 9 grains (0·6 g.) daily was prescribed, and with this treatment the improvement was maintained during the next few months. He was able to look after his own home but he did not return to work; the heart rhythm remained normal and the blood pressure was maintained at about 175/120.

In March 1943, while at some dog races, he was seized with an agonizing pain in the chest and left arm. He lost consciousness for about half an hour, and after recovery complained that the left arm felt numb and useless. He was taken to a hospital nearby, where, on admission, the left hand was found to be cold and limp though movements at the shoulder were preserved. The state of the radial pulse was not recorded. Two hours later a detailed examination was made; the left hand was now warm and perfectly normal. While in hospital the cardiovascular findings were as follows: pulse 74–130, sometimes irregular; B.P. 110/90; heart enlarged to the left with double aortic murmurs; no congestive failure; sinus rhythm with a rate of 74 a minute. He was discharged after eight weeks.

We saw him two months later. During this time he had been without quinidine and had noticed a return of the palpitation. On examination, the pulse was 140 a minute and regular, but by contrast with our earlier observations the blood pressure in the right arm was now 110/90 and in the left arm 110/100, while in the aortic area the heart sounds were completely replaced by to and fro murmurs. There was no pulmonary congestion or peripheral œdema. There was 2 : 1 auricular flutter; X-rays of the chest showed slight increase in the diameter of the lower thoracic aorta but no other significant change (Fig. 2, B and C). It was at this time that we realized that our original diagnosis had been incomplete; the man had a dissecting aneurysm and the recent episode was a second dissection. He was readmitted and again normal rhythm was restored after a few days' treatment with digitalis. Quinidine



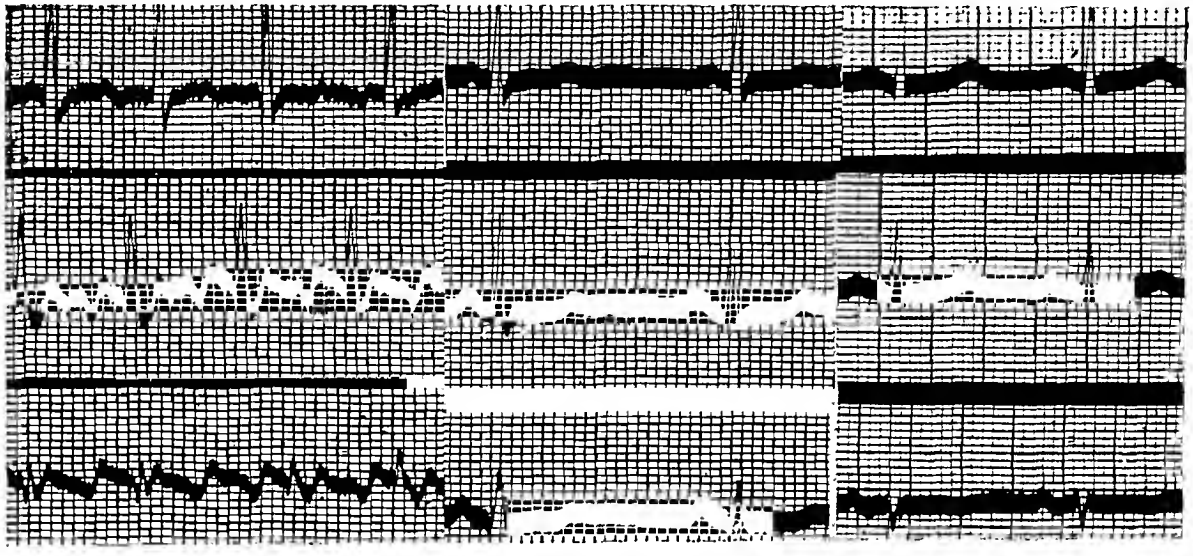
A B C

FIG. 2.—Radiograms of the chest.

(A) 16/10/42. Postero-anterior view, showing the dilatation of the arch of the aorta and the lower thoracic aorta extending to the right of the right border of the heart.
(B) 15/7/43. Postero-anterior view after the second dissection, showing slight increase in the size of the lower thoracic aorta.
(C) 15/7/43. Right (I) oblique position after the second dissection.

therapy was reinstituted and subsequent cardiograms showed a sinus rhythm with low voltage T waves (Fig. 3, C).

He was discharged after two weeks, but from this time could only lead a semi-invalid life. He was often severely breathless and from time to time complained of a " boring " pain in the back of the chest. The physical signs and blood pressure remained essentially unchanged. In July 1944, early congestive cardiac failure developed and he was readmitted for a few weeks. He improved slightly, but after discharge the signs of failure steadily increased. In the evening



A B C

FIG. 3.—Electrocardiograms. Reduced to nine-tenths.
(A) 5/10/42. Showing 2 : 1 and 3 : 1 auricular flutter.
(B) 16/10/42. Sinus rhythm with slight depression of S–T I and S–T II compatible with digitalis therapy.
(C) 16/7/43. Sinus rhythm with low voltage T waves and slight inversion of T III.

of 20/12/44, after unusual exertion, he suddenly developed a very severe continuous pain in the back; it regressed to some extent, but a few hours later he died suddenly.

By the courtesy of the coroner for Westminster, we were able to attend the post-mortem examination. There was a partially healed dissecting aneurysm of the aorta, which had ruptured into the right pleural cavity.

Post-mortem findings

The heart was enlarged and the walls of the left ventricle were hypertrophied; the heart valves and the coronary arteries were healthy. In the aorta there was an elliptical opening in the intima 5 cm. above the aortic valves extending two-thirds of the way round the right and posterior aspects of the vessel. This orifice led backwards towards the heart into a large sac, filled with organized thrombus and lying in front of the superior vena cava and the right auricle. Viewed from the auricular aspect the sac was bulging into the cavity of the right auricle in front of the superior caval opening. From the elliptical tear the dissection wound spirally upwards in front of the ascending arch of the aorta, to reach the posterior aspect of the descending part of the arch, and in so doing the origins of the great vessels arising from the arch were dissected up 2–3 cm. The spiral direction of the dissection continued, the aneurysm lying on the posterior and the right aspects of the thoracic aorta, and it had ruptured back into the abdominal aorta, which was atheromatous, just above the bifurcation.

Throughout, the dissection occupied two-thirds of the circumference of the aorta, the true aorta appearing as a narrow tube attached to the larger dissecting aneurysm. Just above the diaphragm the aneurysm formed a saccular dilatation extending into the right pleural cavity. In this sac there was a longitudinal rent, 3 cm. in length, where the external rupture which caused his death had occurred. The walls of the aneurysm were covered with a pearly white

tissue resembling endothelium, with here and there partially organized adherent thrombi. The other organs showed no significant changes.

Discussion

The radiological appearance of the aorta remained essentially unchanged during the period this patient was under observation, and it is on this evidence that the diagnosis of silent dissecting aneurysm was made. The classical features of aortic dissection were only present during and after the second attack, and it seems likely that on this occasion the great vessels arising from the arch of the aorta became involved in the dissection, for the abnormal blood pressure readings found subsequently were evidence of new and permanent interference to the blood flow in the upper limbs.

The significance of the cardiac arrythmia found when this man was first seen is not entirely clear, but its presence supports the view that he had at that time a dissecting aneurysm. Abnormal heart rhythm has not often been reported in aortic dissection, probably because the common early fatal termination precludes cardiographic studies. In an extensive search we have found only one other report of auricular flutter associated with dissecting aneurysm (Mote and Carr, 1942), and other arrythmias are also rare. The saccular dilatation at the base of this patient's aorta encroached on the region of the sinus node and must have interfered with the mechanics of the right auricle. We therefore think the aneurysm was responsible for the auricular flutter, though, if this was so, it is remarkable, in view of the gross anatomical disturbance in this area, that digitalis and quinidine were able to control the abnormal rhythm.

Painless dissections of the aorta are rare episodes in a rare disease. In most of the reported cases the aneurysms have been limited in extent or they have failed to involve any of the great vessels arising from the arch of the aorta (Wedd and Thomas, 1932; Weiss, 1940; and Reich 1944). Sometimes the dissection has occurred during sleep and unconsciousness has supervened so rapidly that no complaint of pain could be made (Jessiman, 1939). In our case the original dissection was unusually extensive; it had probably involved the ascending aorta and from the X-ray appearances it is clear that the arch and the whole thoracic aorta were also affected. The absence of any history of anginal pain and the presence of hypertension in the arm suggest that this dissection had caused no interference with the blood flow in the coronary arteries or the great vessels arising from the aortic arch.

The pain of dissecting aneurysm has been ascribed to rapid distension of the adventitial tissues of the aorta by the effused blood and it has been thought that it may be absent if the dissection takes place slowly. In many cases, however, the pain, though severe, is limited to one arm or to both lower extremities, and in a few instances it has been indistinguishable from that of coronary thrombosis (Wainwright, 1944). Post-mortem examination in these cases has shown that the main limb vessels or the coronary arteries respectively have been involved in the aortic dissection. It is probable, therefore, that ischæmia is partially responsible for the pain and that in those rare cases where the coronary blood flow and the blood supply to the limbs is unimpaired, pain may be absent or inconsiderable.

For the majority of patients with dissecting aneurysm of the aorta no medical treatment can alter the fatal outcome. In a small number where, as in the case we have described, rupture back into the general circulation has taken place, complete rest in bed may relieve strain on the aneurysm wall and promote healing of the dissection. Subsequent management along the lines adopted for cardiac cripples does provide some hope of a return to partial activity.

Summary

A case of recurrent dissection of the aorta with auricular flutter is described.

The first dissection was silent and was survived for over two years; the second presented the characteristic syndrome, and the patient died eighteen months later.

The cause of pain in dissecting aneurysm is discussed.

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THE GENESIS OF THE NORMAL ELECTROCARDIOGRAM

BY

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Received March 28, 1946

The argument of this paper is based on the great work of Lewis, and all references to "Lewis, 1925" are to the third edition of *The Mechanism and Graphic Registration of the Heart Beat*. His demonstration (confirming Engelmann, 1875) that the contraction wave passes through cardiac muscle from the point of stimulation in all directions with equal velocity (p. 84); his considered view of the direction of the spread of the excitation wave in the human ventricles (diagram, p. 115); his table of synchronous events (p. 47); and his statement that the direction of travel of the contraction wave is of more importance than the disposition of contracting and resting masses of muscle in determining the form of the electrocardiogram (p. 57, footnote) are of fundamental importance.

In this paper two other points are emphasized: that air-filled lung is practically an insulator; and that the laws of composition and resolution of mechanical forces do not apply to electrical currents. On these concepts an explanation differing in some respects from that given by Lewis is founded.

The Fundamental Principle

If a battery, packed in insulating material, is placed inside a hollow shell of conducting material, with its positive and negative poles connected, through resistances p and n, with areas P and N on the inner surface of the shell, a current will flow from P to N through the wall of the shell in all directions (Fig. 1). If the terminals of a voltmeter are applied to any two points, A and B, on the surface of the shell, the voltmeter will register the difference of potential between them.

The heart is a battery: it is packed in insulating material, air-filled lung; its positive and negative plates are the anterior and posterior faces of an advancing contraction wave; and p and n represent the resistances of the conducting tissues leading from these "plates" to the wall of the thorax. The thorax is a hollow, hemi-ellipsoidal shell whose walls are made of conducting materials, viz. blood-filled muscles and, through the diaphragm, the liver. P and N are the most positive and negative points on the surface—the surface poles—and the string galvanometer is for all practical purposes a voltmeter, as it is standardized before each lead to register volts, not amperes.

Intrinsic and Surface Voltage

The difference of potential between two points on an electrical circuit is proportional to the resistance between those points. The total resistance of the circuit from the + plate to the − plate is $p+s+n$, where s is the resistance of the shell. If V is the potential difference between the plates—the intrinsic voltage of the battery—then the potential difference, E, between the surface poles P and N—the surface voltage—will be $V\left(\frac{s}{p+s+n}\right)$. If s is constant the relation of E to V depends on the values of p and n; if either is large, E will be small. But if these are constant and s variable, a decrease in s will diminish the ratio $\frac{E}{V}$

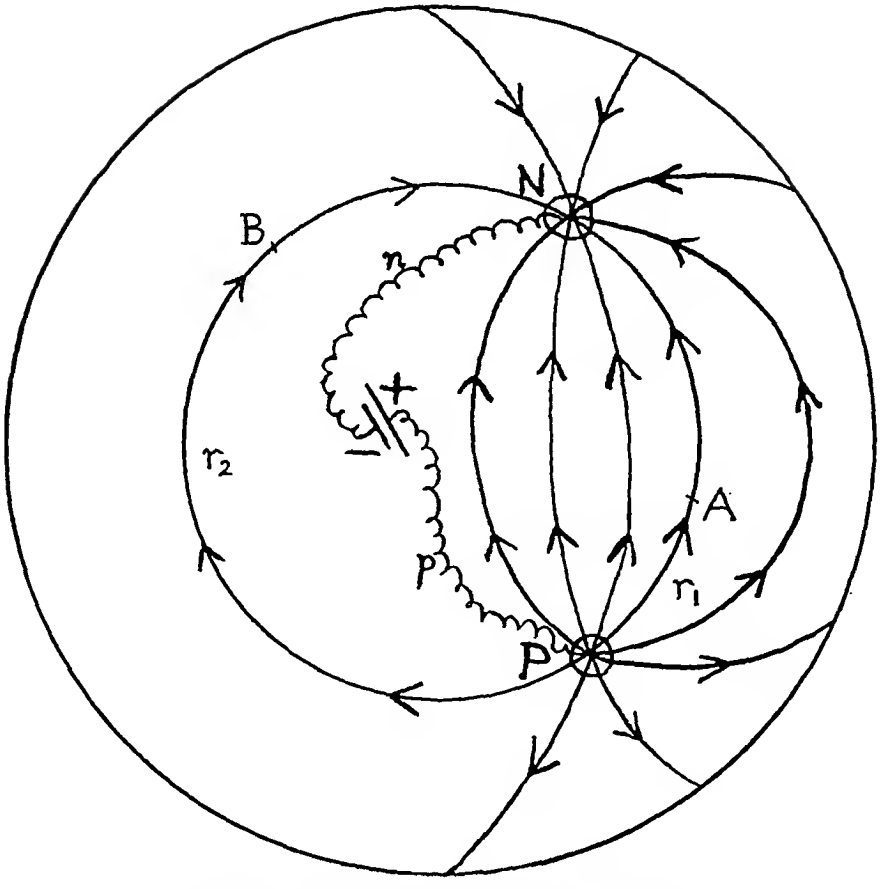

FIG. 1.—Diagram of a battery enclosed in a hollow shell.

+ − Positive and negative plates of battery.
P, N. Positive and negative " surface poles."
p, *n*. Resistances between plates and poles.
A, B. Points on the surface of the shell, connected by a voltmeter (not shown in diagram).
r_1. Resistance between P and A on circuit P–A–N.
r_2. Resistance between P and B on circuit P–B–N.

It can be shown mathematically that the resistance of a hollow metal sphere of uniform thickness and conductivity is practically constant wherever the poles are applied, unless they are very close together. If Fig. 1 represents a sphere of 36 in. circumference, and P and N are circular areas 2 in. in diameter, the resistance *s* will vary by less than ±10 per cent from a mean value so long as the centres of P and N are not less than 4·5 in. apart. But at 3 in. the resistance is halved, and at 2 in. it is zero; for then the edges of P and N are in contact and the current is short-circuited without passing through the shell.

It will be seen that low surface voltage, without change of intrinsic voltage, may be due to poor contact between the heart and the chest-wall at one or both of the poles, to proximity of the surface poles, and to internal short-circuiting. These account for the low voltage of some phases of the normal cycle.

In pathological conditions low surface voltage (i.e. low voltage in all leads, including the most favourable chest lead) is sometimes thought to be evidence of degeneration of the myocardium or of interference with its function, e.g. by tamponnade. This is not necessarily the case. In advanced emphysema the interposition of a pad of lung between the heart and the chest wall may cause very low surface voltage for many years before there is any sign of heart failure. Pericardial effusion may have the same effect. It is possible that the low voltage associated with manifest heart failure may sometimes be due to the presence of fluid in the pericardium.

It will also be seen that the " surface zero "—the potential intermediate between P and N —bears no fixed relation to the " intrinsic zero." If $n>(s+p)$ the whole surface of the shell, including N itself, must be positive. No point or combination of points can be found on

the body that will give a true zero potential, or will be at the same potential throughout the cycle, or will be at the same potential at the same phase of the cycle in different patients. The various forms of two-point and three-point lead may prove clinically useful, but they do not give absolute voltage values, comparable from patient to patient, and it would surely be advisable to avoid terms that suggest that they do, such as unipolar lead, voltage lead, indifferent point, etc.

Potential distribution in the Normal Cycle

Fig. 2 to 6 and 8 show the main features of the potential distribution on the chest, with diagrams of the corresponding events in the heart. In constructing the diagrams of ventricular excitation the time-relations given by Lewis (1925) have been followed. The contraction wave is shown in the diagrams as a line between shaded and unshaded muscle. The shaded area is in contraction, and is conducting negative electricity from the posterior face of the wave; the unshaded part is about to pass into contraction, and is conducting positive electricity from the anterior face of the wave; arrows show the paths of conduction. In the surface charts the shaded areas are positive, the stippled areas negative; the poles are shown as clear spaces with a + or − sign.

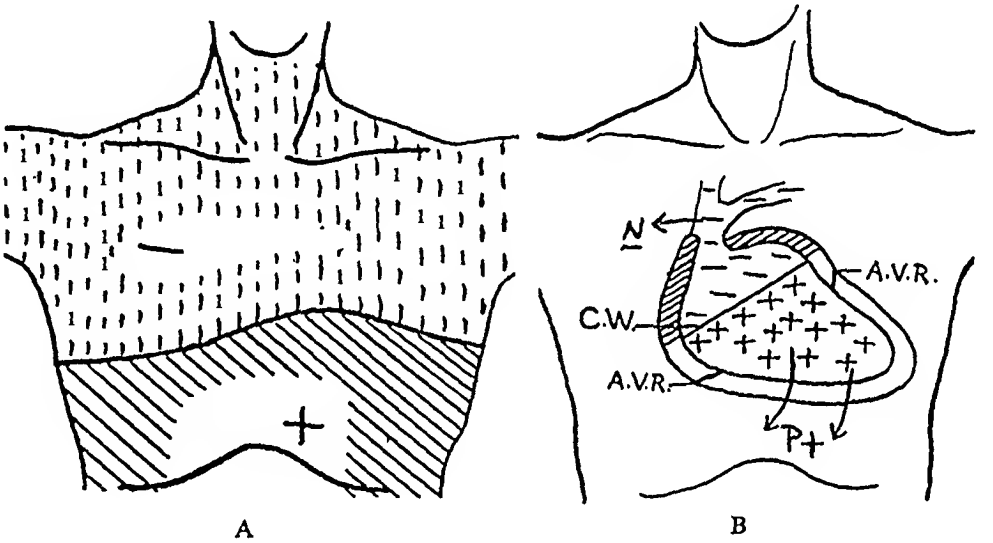

Fig. 2.—The P wave.

(A) Potential distribution on chest.
(B) Electrical events in the heart. A.V.R., auricular-ventricular ring. C.W., contraction wave. P, N, surface poles.

In Fig. 2B the wave has passed half-way down the auricles; these have begun to contract, and a wave of distension is starting to travel backwards from the superior vena cava. This distension wave reaches its maximum in the jugular veins during the inscription of QRS (Lewis, 1925)—the *a* wave of the polygram. It forms the negative pole. At the present stage its contact with the chest wall is poor—resistance *n* is large—and the surface voltage is low. There is also free internal short-circuiting through the intra-auricular blood.

In Fig. 3 the stimulus reaches both sides of the septum simultaneously. Both surfaces become negative, and there is no conduction path for the positive electricity in the interior to the chest wall except down the septum to the apex, where the positive pole is in immediate contact with a negative area that surrounds it. Shell resistance, *s*, is therefore minimal, and the surface voltage so low that there is no deflection.

The stimulus next reaches the papillary muscles (Fig. 4). There is not much short-circuiting, but again the poles are close to one another and the surface voltage is low.

The stimulus now strikes the endocardial surface of both apices and travels up both arborizations (Fig. 5 and 6). If the stimulus passes along the arborisation with velocity *a*, and at every point as it passes starts a contraction wave which spreads radially with velocity

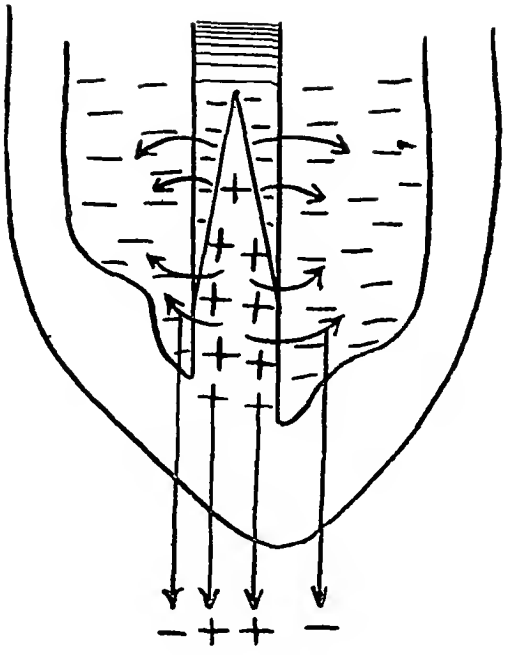

FIG. 3.—Stimulation of ventricular septum.

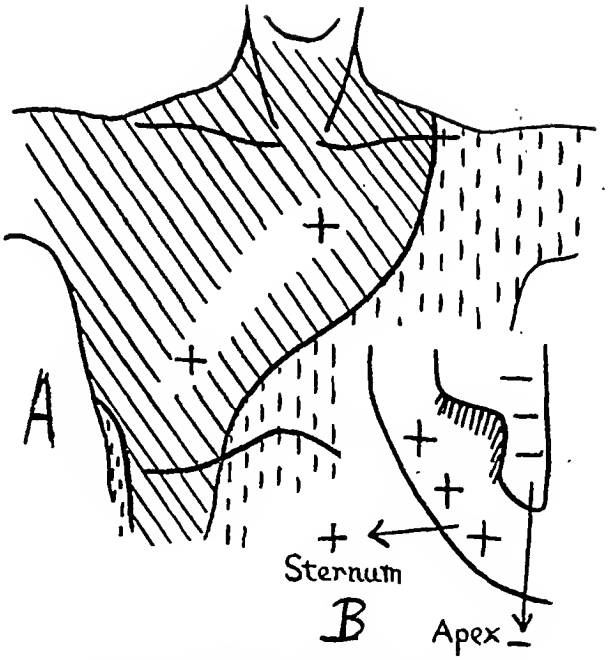

FIG. 4.—Stimulation of papillary muscles. (A) Potential distribution during inscription of Q. (B) (inset) Corresponding electrical events. The negative pole (not shown because of the inset) is at the apex.

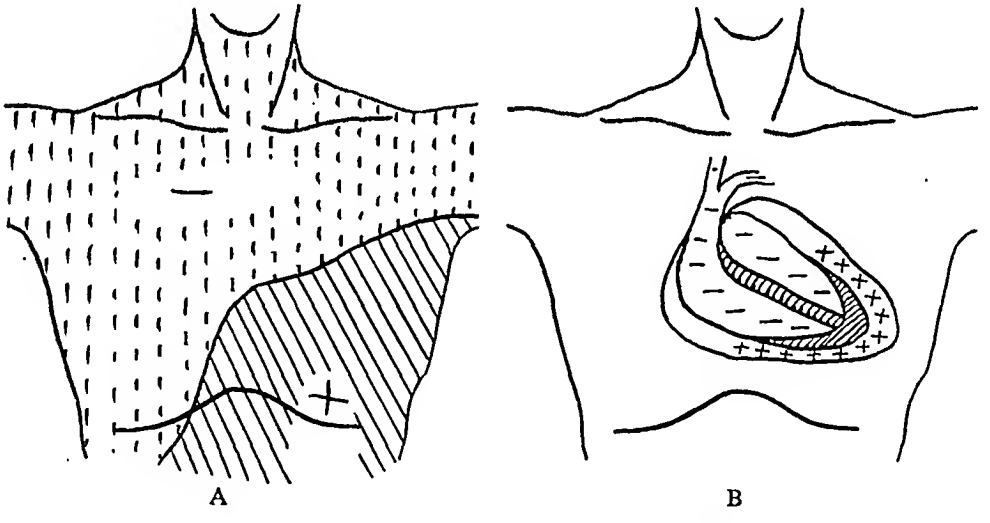

FIG. 5.—The first part of the RS deflection. (A) Potential distribution. (B) Electrical events.

c, the net result is a continuous contraction wave travelling away from the endocardium at an angle whose tangent is *a*/*c*. Meanwhile the distension wave has reached the innominate veins and is spreading across behind the manubrium from right to left. Both poles are now in close contact with the chest wall, and are not close together. *p* and *n* are small, *s* is large; the ratio E/V is at its largest and the surface voltage is high.

The left ventricle is thicker than the right, and the contraction wave takes a little longer to pass right through its wall. The effects of this are shown in Fig. 6.

On this view, septal contraction takes place during the last part of the P–R interval, the phase of silent activity. Comparison of normal and abnormal complexes in the same lead from the same patient shows that in the " short P–R, B.B.B. syndrome " (Hunter, Papp, and Parkinson, 1940) the part of the QRS deflection that precedes the notch does actually occupy this period. The features of this syndrome may be explained by supposing that there is a

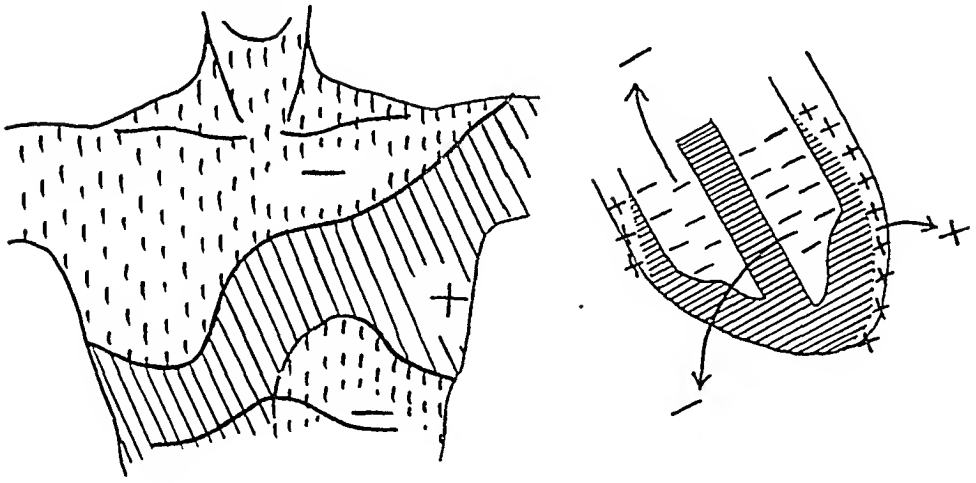

FIG. 6.—End of QRS deflection. Potential distribution and electrical events at the end of R I.

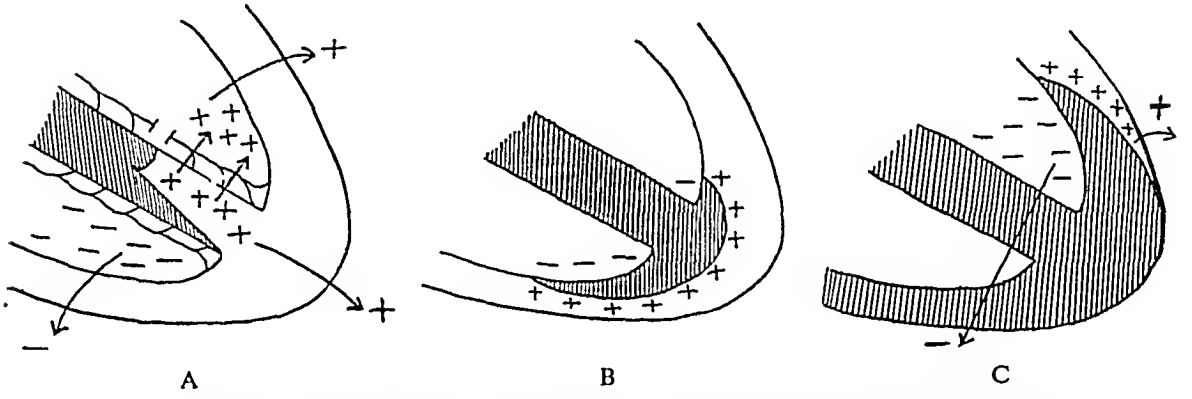

FIG. 7.—Sequence of electrical events during inscription of QRS in organic left bundle branch block. (A) The initial deflection. (B) The "notch." (C) End of the deflection.

shorter or longer delay in the passage of the stimulus down the left bundle branch. The first deflection is then due to unilateral stimulation of the septum; the form of the rest of the complex depends on the degree of asynchronism. Fig. 7 shows the sequence of electrical events in organic left bundle branch block; it is easy to see that these would give the typical electrocardiogram. This explanation has been suggested elsewhere (Hill, 1939) and independently by Roche (1945).

THE T WAVE

The only mystery of the T wave is its direction. When a strip of cold-blooded muscle is stimulated at one end the contraction wave deflection is followed after an interval by an anabolic wave deflection which is flatter, broader, and opposite in direction. The T wave follows the ventricular contraction wave after an interval, and is broader and flatter, but not necessarily in the opposite direction. There can be little doubt that it is anabolic; it is modified by many conditions that are known to affect anabolism—asphyxiation, ischæmia, diabetes, etc. Moreover, a ventricular extrasystole can occur immediately after it, or even during its downstroke, but never before it. This proves that some degree of anabolism occurs during its inscription.

But there is one form of T wave that does follow the pattern of the muscle strip—the T wave of a ventricular extrasystole; it is broader, flatter, and always in the opposite direction to the primary deflection. That it is an anabolic wave is proved by the fact that another ventricular extrasystole can follow immediately after it.

In the auricles mechanical contraction, i.e. diminution of cubic capacity with expulsion of contents, follows almost immediately on the electro-chemical event that causes the P wave; in the ventricles mechanical contraction begins during the S–T interval. Lewis' table of

synchronous events shows that the inscription of QRS is completed before the aortic valves open; QRS is synchronous with a sharp rise of intra-ventricular pressure to the level of the aortic pressure. During, and for some time after, this period the ventricular walls are put on the stretch, and the blood is squeezed out of them (systolic blanching can easily be seen in the exposed frog's heart). Shortly after the opening of the aortic valves the pressure in the aorta rises rather higher than in the ventricle; it is at this point that the T wave begins, and its peak coincides with the maximum difference of pressure at this stage. It comes to an end shortly before or after the aortic valves close ; the U wave accompanies the dicrotic rise in the aorta.

The distinctive feature of a ventricular extrasystole is that it causes little rise of intra-ventricular pressure; the walls do not become ischæmic, and the anabolic wave is able to follow its natural course in the wake of the contraction wave. With a normal contraction, anabolism is prevented by ischæmia; it has to wait for the return of blood, which penetrates inwards from the coronary vessels on the surface. It therefore travels in the opposite direction to the contraction wave, and, being of opposite sign, gives a similar deflection. It travels relatively slowly compared with the contraction wave, and most of the time the whole of both ventricles is taking part in it. Distension of the pulmonary artery and re-expansion of the right auricle give a wide distribution of negative potential, different from that obtaining during inscription of QRS, so that the T wave is not an exact copy of it in every lead (Fig. 8).

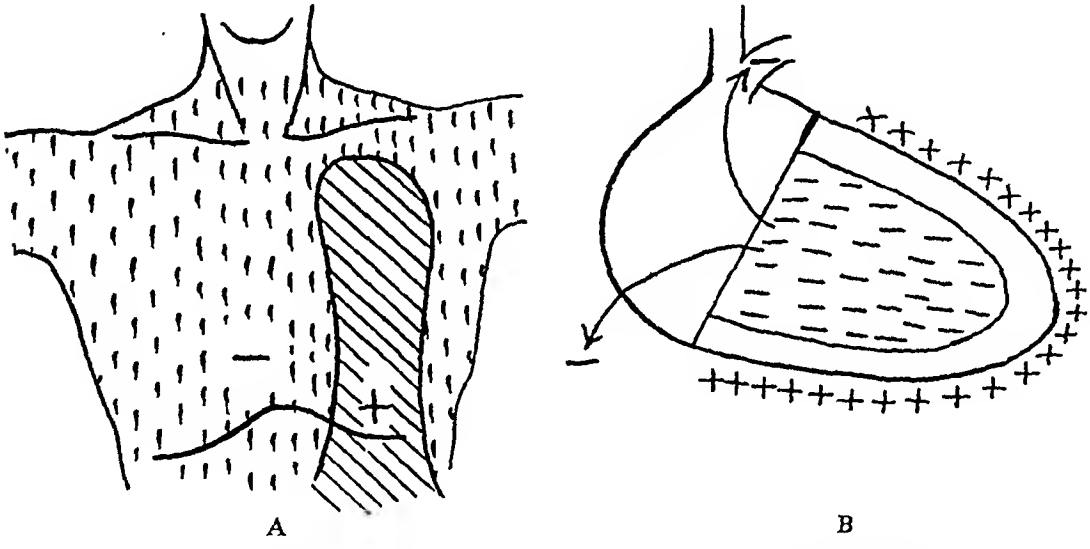

FIG. 8.—Peak of T wave. (A) Potential distribution. (B) Electrical events.

In short, the explanation offered is that the return wave of a ventricular extrasystole is the " natural " anabolic wave, and the normal T wave is the same thing modified by intra-ventricular pressure. When the aortic pressure during diastole is high and the left ventricle is beginning to fail its wall may be so much stretched that the coronary return is delayed till relaxation is far advanced; the T wave is then diphasic. Reduction of peripheral pressure by trinitrin reduces the intraventricular tension, and the T wave may then become upright and normal.

Delay of anabolism of the left auricle by intra-auricular tension may perhaps account for the onset of flutter or fibrillation in mitral stenosis.

INSCRIPTION OF DEFLECTIONS

In the normal subject there is a point at the costal margin, about three inches to the left of the middle line of the back, that is iso-electric with the standard left leg contact throughout the cycle. The left leg contact is virtually attached to the thorax at this point; similarly the forearm contacts are virtually attached to the thorax high up in the axillæ, the arms functioning simply as additional lengths of wire of low resistance.

It is convenient to think of the conduction paths between the surface poles, P and N, as

an infinite number of separate circuits lying side by side. Fall of potential between two points on a circuit is proportional to the resistance between those points. In Fig. 1, if E is the potential difference between P and N, R_1 the resistance of the circuit P–A–N, and r_1 the resistance of that part of it lying between P and A, the fall of potential from P to A is $E(r_1/R_1)$. If, by a similar notation, the fall of potential from P to B is $E(r_2/R_2)$, the potential difference between A and B, registered by the voltmeter, will be $E(r_2/R_2 - r_1/R_1)$.

The positions of the surface poles during inscription of R in lead 1 are shown in Fig. 5A. The negative pole moves leftward to the position shown in Fig. 6, following the backward movement of the distension wave along the innominate vein. In Fig. 9 the left axilla corresponds with A in Fig. 1, the right axilla with B. Since the conducting musculature is much the same on both circuits it is clear that r_2/R_2 is at first much greater than r_1/R_1; conse-

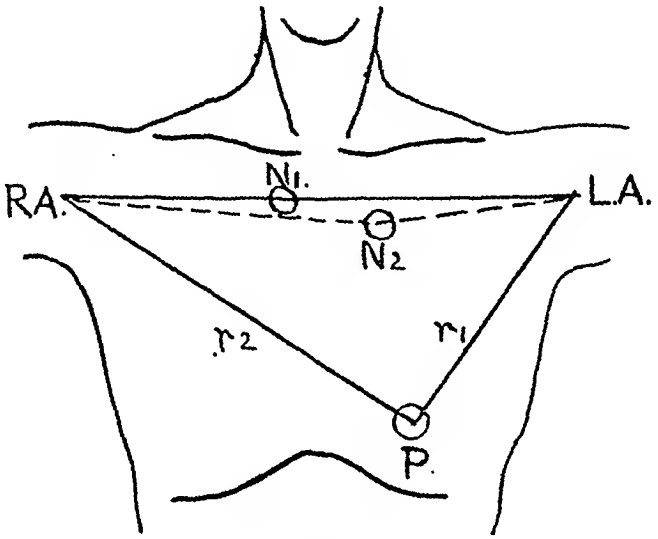

FIG. 9.—Diagram illustrating inscription of R I.

quently L.A. will be strongly positive to R.A., and there will be a large upward deflection. But as N moves leftward from N_1 to N_2, R_2 increases at the expense of R_1 while r_1 and r_2 remain unchanged. The difference between L.A. and R.A. therefore diminishes and the deflection falls back to the base line. A little further movement of N to the left would invert it.

Second and third lead deflections are determined by the same principles, but as the conduction paths from the left leg point pass through the dorsal muscles their amplitude and direction vary with the shape and muscular development of the chest.

ELECTRICAL AXIS

It is not too much to say that the whole doctrine of electrical axes, resultant and component currents, right and left preponderance, summation of currents, equilateral triangles, etc. is quite untenable and must be abandoned. The direction of an electrical current is determined solely by the conducting paths available and has no relation to the orientation of the battery in space. Electrical currents do not " sum " unless their sources are connected in series—the negative pole of one to the positive pole of the other and vice versa. When connected in parallel the voltage is intermediate between that of the two sources, the exact value depending on the arrangement of resistances, external and internal. Simultaneous occurrence of an auricular contraction and a ventricular event is equivalent to connection in series (combine Fig. 2B with Fig. 5B or 8B); the P wave appears superimposed unchanged on the QRS or T. But the two ventricles are connected in parallel, having a negative contact in common and a continuous positive pole (Fig. 5B and 8B); it is impossible that their voltages should be added.

It is true that if the ends of a diameter of a mass of conducting material are maintained at a potential difference V, a voltmeter applied to the ends of other diameters will show intermediate voltages resembling the components of a mechanical force; but the law determining

their magnitude would depend entirely on the shape of the conducting mass. A component of a mechanical force is proportional to the cosine of the angle between its direction and the line of the force, but this would be true of electrical components only if the mass were a straight rod of uniform cross-section. If the mass were a sphere the voltmeter would show a voltage equal to $kV \cdot \log\left(\frac{1+\cos A}{1-\cos A}\right)$; with other shapes other rules would hold good.

But when we recognize that air-filled lung is almost an insulator the picture becomes that shown in Fig. 1. Here the orientation of the battery matters not at all; all that matter are the points at which the paths of least resistance from the plates of the battery most nearly approach the inner surface of the conducting shell. These become the surface poles, and potential distribution then follows the ordinary laws of conduction through the walls of the shell.

It is, then, difficult to assign any precise meaning to the term electrical axis; but right and left axis deviation are convenient labels for two contrasted types of electrocardiogram.

Left axis deviation. The tall R I and deep S III indicate that at the peak of the QRS deflection the left axilla is strongly positive to the other two contacts; (similarly, the deep S I and tall R III of R.A.D. show that the left axilla is strongly the most negative of the three). Left axis deviation is common with enlargement of the ventricles, but has never been satisfactorily correlated with preponderance of the left ventricle (Lewis, 1928). All that is necessary for its appearance is that the positive pole, formed by the apical halves of the ventricles, shall be electrically closer than usual to the left axilla. The mere anatomical displacement of the apex is enough to secure this, but when the heart is much enlarged collapse of the base of the left lung must contribute to the effect.

The natural electrical action of the heart was imitated in a series of experiments by applying the poles of a battery (with suitable precautions) to various points on the chest of a subject attached to an electrocardiograph and noting the deflections resulting.

In the first experiment the negative pole was fixed to the middle of the sternum at the level of the second space. Applying the positive pole to the apex beat gave a large upward deflection in lead I and also in lead III; their relative amplitudes were comparable to those of R I and R III in the subject's standard cardiogram. Moving the positive pole to the sixth rib in the anterior axillary line inverted the deflection in lead III, giving the picture of L.A.D. Moving it inward, by centimetre steps, horizontally from the apex to the middle line gave smaller and smaller upward deflections in lead I, but no S I appeared till the middle line was crossed.

Fig. 10A, from a patient whose heart was seen by X-rays to be absolutely vertical and centrally placed, shows that this procedure is a fair imitation of the natural event. The first lead deflections are tiny, but not inverted.

A positive pole at the sixth rib in the anterior axillary line will give the picture of L.A.D.; a natural positive pole is in this position when the ventricles are enlarged; is any more elaborate explanation necessary?

Right axis deviation. When this is present the right ventricle is nearly always hypertrophied, but the converse is not always true. In the early stages of mitral stenosis and in advanced emphysema there may be right ventricular hypertrophy without a trace of R.A.D.

In the course of the experiment described above the conditions that would obtain in "right preponderance" were imitated in an exaggerated form. The positive pole was applied to points on the chest over the right ventricular contact, the voltage was at least ten times as great as the intrinsic voltage of any heart, and there was no positive pole at the apex to represent the left ventricle; yet no downward deflection could be produced in lead I as long as the negative pole was in the middle line.

In the second experiment conditions were reversed. The positive pole was fixed at the apex-beat and the negative pole moved to the left, centimetre by centimetre, at the level of the second space. The upward deflection in lead III increased rapidly, but in lead I it decreased, and at 4·5 cm. from the middle line it disappeared; 1 cm. further to the left gave a deep S I and a tall R III—the picture of R.A.D.

The same result was obtained with the positive pole 4 cm. to the left of the apex in the fifth space, the point of no deflection being 5 cm. from the middle line.

It is clear, then, that a negative pole a very little further to the left than the natural negative pole at the end of the normal R I will give a downward deflection in lead I; and there are two structures in this position, conductors of negative electricity at this stage, which, when dilated, come forward to approach the thoracic wall—the left auricular appendage and the pulmonary artery. The role of a dilated pulmonary artery was suggested by Dr. John Parkinson; it brings the R.A.D. of infundibular stenosis into line with this theory (O'Farrell, 1938).

When these structures are dilated the right ventricle is always hypertrophied, but again the converse is not always true. In early mitral stenosis the right ventricle may be enlarged before much dilatation of the left auricle and pulmonary artery is evident; in emphysema the appendage is not dilated, and the artery is covered by a pad of distended lung.

Fig. 10B affords an indirect confirmation of this view. The patient was a man of 31, with perfectly normal heart, arteries, and blood pressure. In the second left space was a pulsating tumour; the maximum pulsation was 7 cm. from the middle line, dulness to percussion extended 2 cm. further to the left and down into the third space. X-rays showed a solid tumour in contact with the base of the left ventricle and moving with it. The cardiogram shows extreme left axis deviation, but the peaks come rather later than usual, and coincide with the moment when the stimulus reaches the base of the left ventricle. At this instant positive electricity was conducted from the surface of this area through the tumour to the chest wall at the point of pulsation, making the left axilla strongly positive.

The last experiment described above reproduces the conditions present when the heart is displaced bodily to the left by deformity of the chest wall. Fig. 10C is from such a case.

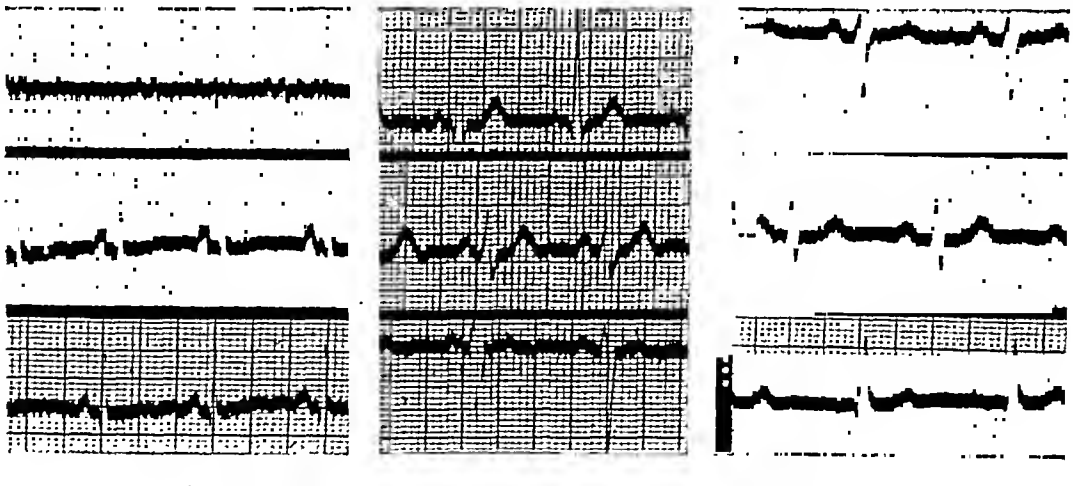

FIG. 10.—Electrocardiograms of: (A) Vertical, centrally placed, heart. (B) Left axis deviation due to an intra-thoracic tumour. (C) Right axis deviation due to displacement of the heart by deformity of the chest. (The second complexes in leads I and III of Fig. 10B have been traced over in Indian ink to facilitate reproduction.) (Reduced to two-thirds.)

X-rays showed no clock-wise rotation of the physical axis of the heart and no sign of hypertrophy of the right ventricle, nor was there any clinical reason to suspect this. The cardiogram shows marked R.A.D.

The argument may be summed up as follows.

1. While the negative pole is in the middle line no voltage applied to the left of the middle line can produce a downward deflection in lead I.

2. A negative pole in the second space 6 cm. to the left of the middle line reproduces the picture of R.A.D. even when the positive pole is to the left of the apex-beat.

3. There are structures, negative during QRS, which when dilated approach the chest wall at this point.

4. When these structures are dilated the right ventricle is always enlarged, but the converse is not always true.

5. When R.A.D. is present the right ventricle is nearly always enlarged, but the converse is not always true.

6. In both cases dissociation occurs in the same circumstances.

7. Exceptionally R.A.D. may be present without rotation of the physical axis of the heart or enlargement of the right ventricle.

8. A pathological positive pole 7 cm. to the left of the middle line in the second space produces extreme L.A.D.

Is it not reasonable to suppose that a pathological negative pole, known to be present in this region, may be the cause of R.A.D.?

Further, is there any direct evidence that the intrinsic voltage of a hypertrophied right ventricle is much greater than that of a normal left ventricle? or indeed of a normal right ventricle? If not, the doctrine of electrical preponderance has no basis whatever.

Salient points have already been discussed in the course of this paper; it only remains to emphasize that anatomical relations and physical principles are of paramount importance in the interpretation of electrocardiograms.

Summary

Fundamental principle. The heart is compared to a battery packed in insulating material and enclosed in a hollow conducting shell.

Intrinsic and surface voltage. The ratio of the maximum potential difference on the surface of the shell (the surface voltage) to the voltage of the battery (the intrinsic voltage) is determined by resistance relations. The low voltage sometimes found in emphysema and with pericardial effusion is thus explained.

Potential distribution in the normal cycle. Charts of this, with diagrams of the corresponding events in the heart, are given for each deflection.

The T wave. The T wave of a ventricular extrasystole corresponds to the secondary wave of a stimulated muscle-strip, and the normal T wave is the same thing modified by intraventricular pressure. Reasons are given for believing it to be anabolic.

Inscription of deflections. The principles determining the direction and amplitude of deflections are explained.

Electrical axis. The laws of composition and resolution of mechanical forces do not apply to electrical currents. Left axis deviation is ascribed to proximity of the positive apex to the left axilla; right axis deviation to an abnormal negative pole between the sternum and the left axilla, formed by dilatation (or occasionally displacement) of the left auricular appendage or pulmonary artery or both. These conditions can be imitated by applying the poles of a battery to appropriate areas on the chest.

Thanks are due to Miss Loveday Hill for invaluable help in preparing the illustrations; and to Sister Lawson, S.R.N., for the photographic work.

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HEART-VECTOR AND LEADS

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Received February 14, 1946

The purpose of electrocardiographic investigation is to find out something about the heart itself by means of an accurate knowledge of its electric action. This may be represented by the so-called heart-vector, a directed quantity, indicating in which direction electricity is propagated by the heart. The amount of each lead at a given instant depends on the heart-vector. The latter changes during the heart beat in direction and magnitude and, consequently, the value of the lead, too, changes with time.

The relation between heart disease and leads is, at the root, very complicated. One can, however, analyse this relation by dividing it into a relation between heart disease and heart-vector and a relation between heart-vector and leads. *The first relation is only to be found on the ground of medical experience. The second relation, on the contrary, is of a purely physical nature, and will be the subject of our discussion.*

A long time ago Einthoven *et al.* (1913) with his so-called triangle rule, tried to formulate the relation between the heart-vector (which he called the manifest potential difference) and the three limb leads. Einthoven himself realized very well that this rule gives only an approximation of the truth. What the significance is of this approximation can be decided only by measurement. We have tried to formulate the physical problem and next to obtain, by measurements on a phantom, the data necessary for the application of the fundamental solution of the physical problem.

The Relation between Heart-Vector and Leads

In the first place one must try to get a clear idea of the heart-vector. The propagation of electricity by an excited muscle has, without doubt, its origin in the electrolytes present in the tissue. By diffusion of electrolytes a potential difference is generated. This can be explained as a consequence of an electric field, acting on the ions. This electromotive field, together with the common electrostatic field, is the cause of an electric current in the electrolyte. In the case of living tissues, the cell-membranes have a preponderating influence on the generation of the electromotive field.

By the excitation of the heart muscle, an electromotive field arises. This is located in the heart muscle and causes a current in it as well as in the trunk around it. The heart muscle is the active part; the conducting tissue of the trunk the passive one. This can be compared to a galvanic cell (heart muscle) with an external resistance (rest of trunk). There is, however, a great difference here, because we have not to deal with a current through a wire, which can be characterized by one single number, the current intensity. In the trunk there is a *current-field.* We can represent this field by drawing current lines, indicating from point to point the direction of the current (Fig. 1). This figure holds only for one single instant, the current-field changing periodically with the heart beat.

Each little piece of the heart muscle contributes to the current-field independently of its other parts. This contribution is proportional to the volume of the small piece and to the intensity of the electromotive field existing in it. The total action of the heart muscle is the result of the actions of all the small pieces.

We must bear in mind that the action of each piece, i.e. its contribution to the total

current-field, depends also on its relative position in the heart. For simplicity, however, we shall for the time being ignore this complication. The current-field will then be determined by the (vectorial) sum of the electromotive field strengths in the different pieces of the heart muscle. This vectorial sum determines, by its direction and magnitude, the current field in the trunk. It is this sum that we have to call the heart-vector.

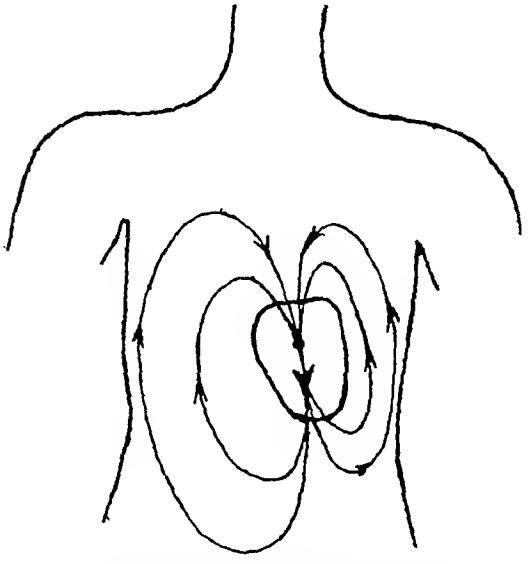

FIG. 1.—Current field in the trunk, caused by the electric action of the heart.

It is possible to give a generally valid relation between heart-vector and current field. The latter is the resultant of the fields that would be set up by the rectangular components X, Y, Z of the heart-vector separately. Each of these fields is proportional to the component by which it is originated. The current field in the trunk gives rise to potential differences between the points at the surface of the body (leads). The relation between these potential differences and the components of the heart-vector is of the same type as that between current field and heart-vector. Each lead, therefore, can be represented by the single equation :

$$\text{Lead} = aX + bY + cZ \quad . \quad . \quad (1)$$

a, b and c depend on the shape, dimensions, and conductivity of the trunk and on the position of the electrodes used. They do not depend, however, on the direction and magnitude of the heart-vector nor, therefore, on its components X, Y, and Z. During the heart beat the heart-vector changes and, therefore, its components X, Y, and Z change too; during this change, the constants a, b, and c remain unchanged.

We need three equations to solve the three unknowns X, Y, and Z, so that we have to measure three independent leads. These three equations contain 9 (3×3) constants of the type a, b, and c.

Between the three limb leads (LR, RF, and FL) there is a relation, their sum being zero, so that they are not sufficient to find the three components X, Y, and Z. In practical electrocardiography, however, the component that points forward is often neglected. The leads LR, RF, and FL would then, theoretically speaking, be sufficient to determine the two components of the heart-vector that are parallel to the frontal plane, but in reality the component that points forward may not be neglected.

The relation between heart-vector and leads may be represented geometrically, but instead of the equilateral triangle according to Einthoven, an oblique triangle has to be used. We shall not enter further into this geometrical representation here, nor shall we explain how the shape of the triangle depends on the coefficients of equation (1).

MEASUREMENTS ON A MODEL OF THE HUMAN BODY

Numerous investigators have tried to study the relation between heart-vector and leads with the aid of a model. They have employed models that were only very rough approximations of the human body. For example, triangular and circular pieces of filter paper, soaked in an electrolyte and glass tanks filled with an electrolyte have been used (Hess, 1935; Hollmann, 1937; Momm, 1933; and Wilson, 1930). It is very important that the flow of electricity through the body is a three-dimensional phenomenon, which cannot be studied by means of the electric current in a flat layer of liquid. The shape of the boundary of the conducting liquid influences essentially the course of the lines of flow. We have used a glass phantom, the shape of which is a copy, as correct as possible, of the human body on a scale of 1 : 3. At the ends of the extremities it is fitted with copper electrodes and it is filled with a diluted solution of copper sulphate. The cranial roof is absent ; through this opening the phantom is filled with the electrolyte and an artificial heart is introduced.

By choosing the correct shape of the phantom, only one requirement is fulfilled, namely, the one of the three-dimensional current. The other requirement is that the specific resistance from point to point, apart from a proportionality factor, be the same as in our body. The mean specific resistances of the different parts of the body do not diverge much, but especially for the trunk these differences are important (Hess, 1935). It is more particularly the lungs, with their high specific resistance, that account for an appreciable lack of homogeneity. In this first paper we shall deliberately neglect this complication and operate with a homogeneous trunk.

As an artificial heart we used two circular copper plates P_1 and P_2, both about 2 cm. in diameter (Fig. 2). These plates are parallel to each other and are connected with the ends of an isolating cylinder of a length of 2 cm. The isolated wires, let through a narrow glass tube B, serve to set up a potential difference between these plates. This potential difference gives rise to a current in the surrounding liquid. Fig. 2 represents a heart, causing a vertical heart-vector. Besides, we used also a heart of which the two plates are put vertically in the standing trunk and by which we can make a horizontal heart-vector act. We have only concerned ourselves with the leads LR, RF, and FL from the extremities. The component of the heart-vector pointing forward is neglected as usual.

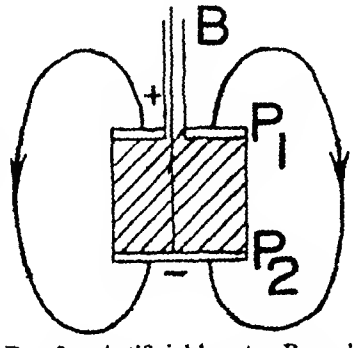

FIG. 2.—Artificial heart. P_1 and P_2=copper plates, being used as electrodes. B=tube, in which are connecting wires.

In the relevant papers we could not find reliable data concerning the position of the human heart. We used, therefore, rœntgenograms. The individual data diverge strongly; we used a mean position.

In our simplified case the relation between the two independent leads from the extremities and the two components of the heart-vector is given by two equations, containing four coefficients. In order to determine these coefficients, we have used successively a horizontal and a vertical heart-vector of equal magnitude. By measuring the two leads in both cases, we are able to calculate relative values for the four coefficients.

There exists, also according to Einthoven's triangle rule, a linear relation between the leads and the components of the heart-vector. This relation can be deduced from the well-known geometrical construction. The coefficients found in this way turn out to be rather different from those found with our model.

Absolute Measurements. So far, we have restricted our attention to the relative values of both the heart-vector and the leads. The question now is to introduce the absolute values. For that purpose we must express the heart-vector as well as the leads in centimetre-gramme-second units or in units connected with these (e.g. volts). The leads are expressed in volts. The heart-vector is the product of an electromotive field strength and a volume. The unit in which it has to be expressed is thus found from the units of field strength and volume. The conception of field strength is connected with that of potential difference in such a way that the field strength is the quotient of the potential difference between two points and their distance. We shall, therefore, express the field strength, as usual, in volts per cm. (volt/cm.). The heart-vector is then expressed in a unit found by multiplying the unit of field strength by the unit of volume, that is, in volt/cm. $\times$ cm.^{3} = volt . cm^2.

It is easy to measure the leads, for the model as well as for the human body, in an absolute unit, i.e. in volts. The absolute value of the heart-vector of the artificial heart is calculated from its dimensions and its potential difference. Taking into account the ratio between the dimensions of the model and the human body, the heart-vector of the latter can be computed.

The maximum value of the heart-vector is reached at the time of the R deflection. With 1 mV. for lead I and 1·5 mV. for lead II, we find a value of about 1 volt . cm.^{2} for the maximum value of the heart-vector. This result, however, does not appeal strongly to us as we are not familiar with the quantity " heart-vector " nor with the unit " volt . cm.^{2} " The mean value of the electromotive field strength in the heart muscle has a more direct meaning for us. This is found by dividing the magnitude of the heart-vector by the volume of the heart muscle.

Taking for the latter 250 cm.^{3} we get for the mean electromotive field 4×10^{-3} volt/cm.

Perhaps even this value has no direct meaning for the reader. But if we assume that at one and the same moment this field strength exists in the whole muscle, we find the potential difference between two " poles " of the heart by multiplying the mean field strength by the diameter of the heart (circa 9 cm.). In this way we find about $9\times4\times10^{-3}$ volt=36 mV.

Influence of the Point of Application of the Heart-vector. The leads caused by the heart-vector depend not only on its direction and magnitude but also on its point of application. We placed the artificial heart there, where, according to the rœntgen data, the " centre " of the heart is situated. The heart, however, is not very small with respect to the trunk. We may, therefore, expect that the contributions of the different parts of the heart muscle to the heart-vector may not simply be added vectorially, as supposed in the preceding. One and the same electromotive field strength, acting in different points of the heart muscle, will give different contributions to a lead. In order to investigate how large these differences are, we put the artificial heart in different places in our phantom. For this purpose we chose not only the centre of the heart, but also the heart apex, the heart base, and the back of the heart. These selected points are situated on the surface of the heart, the last mentioned point lying straight behind the heart centre. The place of these points is found from radiological and anatomical data.

The results for the different places diverge appreciably. They give, however, a too unflattering impression, as we have chosen points on the surface of the heart, that is to say at a maximum distance from the heart centre.

Possible Application to Vector-cardiography

We may conceive the heart-vector as an arrow, drawn from an arbitrary point as origin. During the heart beat this vector varies as to its direction and magnitude and, in doing so, its end describes a curve. This curve is called by Schellong (1936) the vector diagram. This diagram repeats itself almost identically for each heart beat and represents a characteristic property of the heart.

The computation of the heart-vector for various phases of the heart beat is a laborious task. For this reason a direct instrumental method has been developed for visualizing the curve, the vector-diagram, or for photographing it (Hollmann, 1937*b*).

Up to now the vector-diagram, as far as it is determined from limb leads, is found with the aid of Einthoven's triangle rule. As a matter of course, by using our equation (1) we would find a different diagram from the same data. The vector-diagram found depends, namely, on the coefficients in these equations. The true vector-diagram is found by using the correct coefficients. Although our coefficients are not yet the correct ones, our method gives the means to approximate to the truth. In order to apply the correct coefficients in practice, the recording instrument should be provided with a device by which these correct values, found from the experiments on the phantom, are taken into account. The question as to which leads we must chose becomes in this way theoretically meaningless. For to each set of leads belongs a set of nine coefficients. If these coefficients have been taken into account in the recording instrument, we must necessarily find the true vector-diagram of the patient examined, a curve that represents the electric action of his heart. This curve must be independent of the choice of the leads. The latter is restricted only by practical considerations. This idea, however, has not yet been carried out experimentally.

Summary

There exists a linear relation between heart-vector and leads. The coefficients of the equation giving this relation can be determined by measurement on a model of the human body. This is filled with an electrolyte, in which an artificial heart is placed. As the poor electric conductivity of the lungs is not taken into account, the results are open to improvement.

The absolute value of the heart-vector can also be determined (R deflection=1 volt . cm.^{2}).

The influence of the situation of the excited muscle elements is investigated.

From the leads the heart-vector or a vector-diagram can be derived, either by calculation or by direct registration. The vector-diagram can be found from other leads as well as from the limb leads and will then turn out to be independent of the choice of the leads.

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THE HEART IN STERNAL DEPRESSION

BY

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Received June 25, 1946

The place where the apex beat appears on the chest wall depends as much on the symmetry of the thorax as on the size of the heart. A change in the alignment of the spine, the posterior fulcrum of the thoracic cage, in the form of scoliosis, alters the position of the beat. Local deformity of the ribs which form the walls of the cage will do the same thing. Deformity of the sternum, the anterior fulcrum of the thorax, as a cause of displacement of the apex beat has received less attention. The effects of depression of the sternum (pectus excavatum) on the shape and position of the heart have been studied in sixteen adults examined during the past year.

Description of Cases

All sixteen patients had been referred for an explanation of certain signs connected with the heart, with the knowledge that deformity of the chest was present, but without appreciating that the two conditions might be related. In many of them suspicion of heart disease had led to restriction of their physical activities and to a change of design for their future livelihood.

The *symptoms* that had caused the patients to seek medical advice in the first place were

TABLE 1

Summary of Findings in 16 Healthy Subjects with Depressed Sternum

Case No.	Age	Sternal depression	Antero-posterior chest measurement in inches		Radiological findings in anterior view			
			Patient with control in brackets		Translucency of shadow	Apparent enlargement	Outward shift of left border	Scoliosis
1	36	Funnel	4½	(8½)	Absent	Absent	Great	Effective
2	15	,,	5	(8)	,,	,,	,,	Absent
3	57	Cup	5¼	(8½)	Obvious	Moderate	,,	,,
4	19	,,	5½	(8)	,,	,,	,,	,,
5	19	,,	5½	(7½)	,,	,,	Moderate	Incidental
6	29	,,	5½	(8½)	,,	,,	,,	Effective
7	17	,,	5½	(7¾)	,,	Moderate to slight	,,	Absent
8	17	,,	5½	(8½)	,,	,,	,,	Incidental
9	23	,,	5½	(7)	,,	,,	,,	Effective
10	36	,,	5¾	(8½)	,,	,,	Considerable	,,
11	15	Saucer	6	(7)	Slight	Slight	Moderate	Incidental
12	19	,,	6	(7)	,,	,,	,,	,,
13	19	,,	6	(7½)	,,	-	,,	Absent
14	19	,,	6	(7½)	,,	,,	,,	,,
15	19	,,	6¼	(7)	,,	,,	,,	,,
16	31	,,	6¼	(8)	,,	,,	Slight	Incidental

Note. In addition, the apex beat was displaced outwards in every case and a systolic murmur was present. In the anterior view the pulmonary artery was prominent on cardioscopy in the funnel and cup depression, but not in the saucer variety. In the left oblique view the heart shadow was normal or smaller in size, and in each case it extended on to the spine.

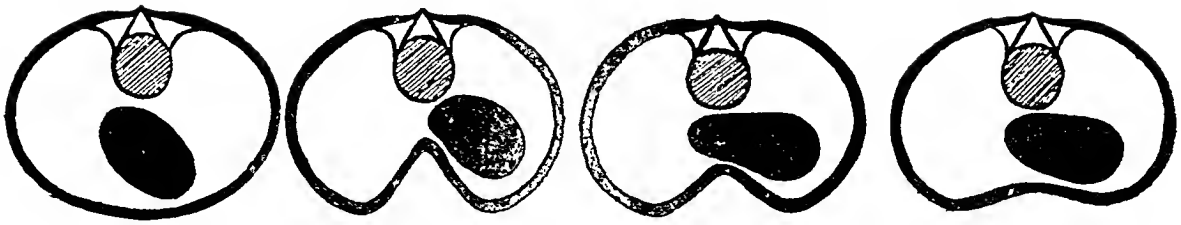

FIG. 1.—Diagramatic representation of the position of the heart in the three kinds of depression of the sternum.

diverse and never the outcome of cardiac embarrassment. In none was there heart failure such as has been attributed to gross deformity of the spine (Coombs, 1930). The symptoms were irrelevant to the condition and were of a general kind such as palpitation, giddiness, tiredness, and lancing pain in the left chest. Of greater importance were the restrictions imposed on the patients, even when symptom-free, because of a routine medical examination. Rheumatic heart disease had been diagnosed in five cases, which were advised to submit to regular medical supervision. Four cases had been relegated to the low health categories of Grade III or IV by Medical Recruiting Boards. Termination of pregnancy had been advised for one. Long periods in bed and absence from her calling as a teacher had been enforced on two occasions in another, aged 57 ; while another, a boy of 19, had been compelled by his medical advisers to discontinue his studies as a medical student; and later was placed in Grade IV

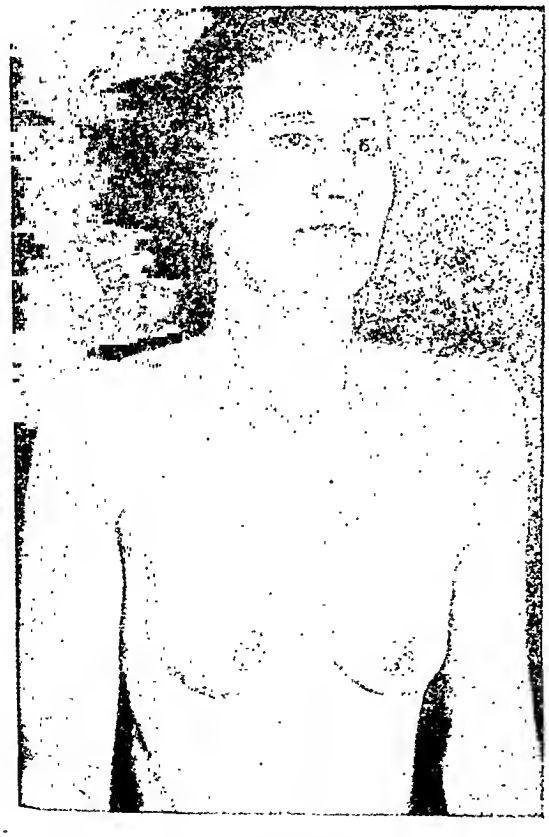

FIG. 2.—Funnel depression in Case 1. Antero-posterior (A–P) measurement of 4¼ inches against 8¼ inches in control.

FIG. 3.—Funnel depression in Case 2. A–P measurement of 5 inches against 8 inches in control.

by three different Medical Boards after an examination that was amplified by a radiologist's report to the effect that there was great enlargement of the heart.

The *physical signs* relate to the sternal deformity and to the altered shape and position of the heart; they have been summarized in Table I.

The sternal depression. It has been conventional to refer to this deformity of the lower end of the sternum as funnel depression, but when the present series was examined it became evident that the effects on the heart depended directly on the extent of the backward bulge of the sternum. Adopting the same simile, three types may be described, the *funnel*, the *cup*, and the *saucer* depression, according to the depth of the sternal pit (Fig. 1). Thus, the funnel type is deep and usually narrow at the apex (Fig. 2 and 3), and the cup variety is moderately deep and usually rounded at the apex, while the saucer type is a shallower and wider depression. The antero-posterior measurement of the chest in the two cases with funnel depression was $4\,1/2$ and 5 inches respectively; in eight cases of cup deformity it varied from $5\,1/4$ to $5\,3/4$ inches, and in the six cases with saucer depression it was 6 or $6\,1/4$ inches. The same measurement for the control series of 16 healthy subjects was never less than 7 inches and the average was $7\,3/4$ inches (Table I). The lateral measurement was unaffected by the sternal deformity and the average of 10 inches was the same for the control series.

The apex beat. This was displaced to the left in all 16 cases; this effect was obvious in the six instances of saucer depression, but it was greater in the ten cases with either cup or funnel depression (Fig. 4 and 5), and in these it often appeared beyond the anterior axillary line. Although scoliosis was present in nine, it only contributed to the displacement in four and even in these in only a small way. In the two cases showing the severe or funnel form of depression the shift of the apex beat had resulted from the escape of the heart to the left away from the grasp of the jaws formed by the sternal bulge and the spine. In the 14 cases with cup or saucer depression the right border of the heart had maintained its normal relationship to the spine, although sometimes it was lifted a little, so that the outward shift of the left

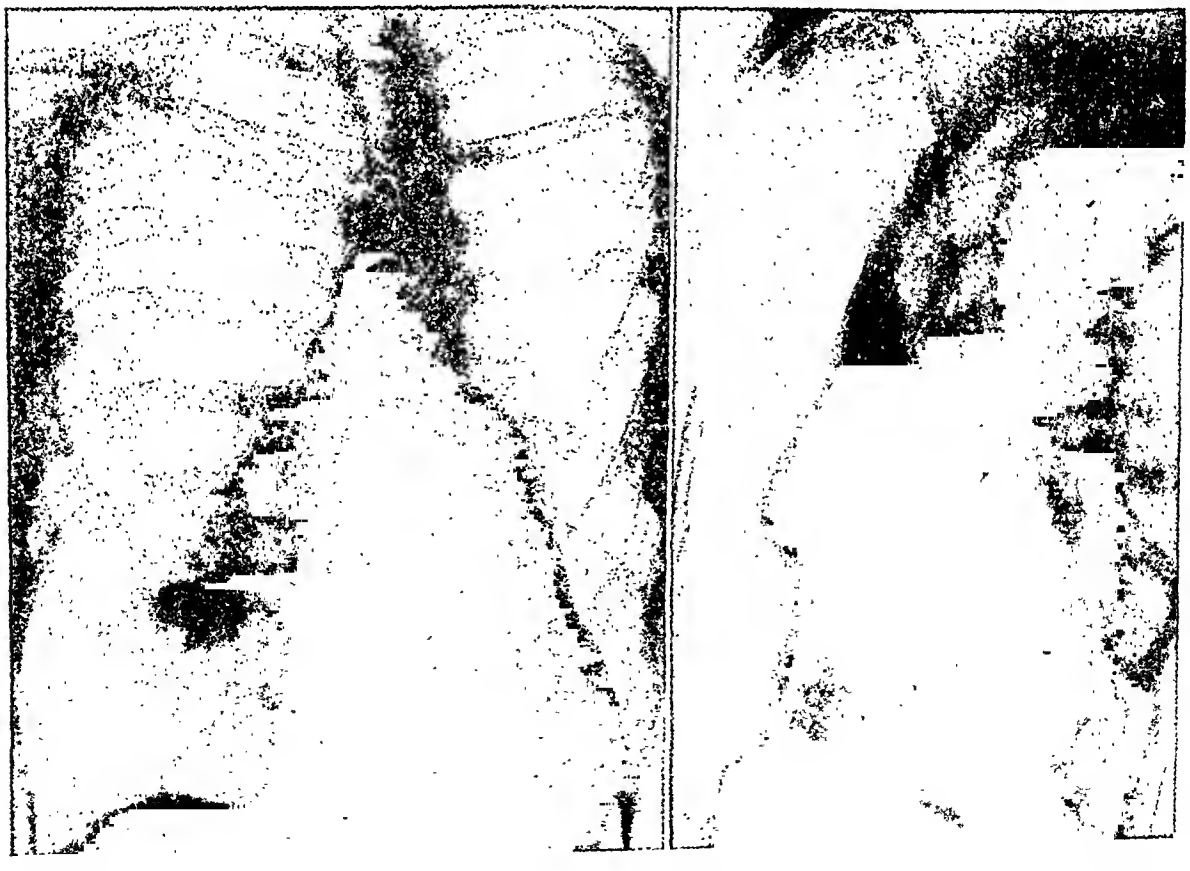

FIG. 4.—Anterior and left (II) oblique teleradiograms in Case 1 with funnel depression. The heart is displaced backwards and to the left.

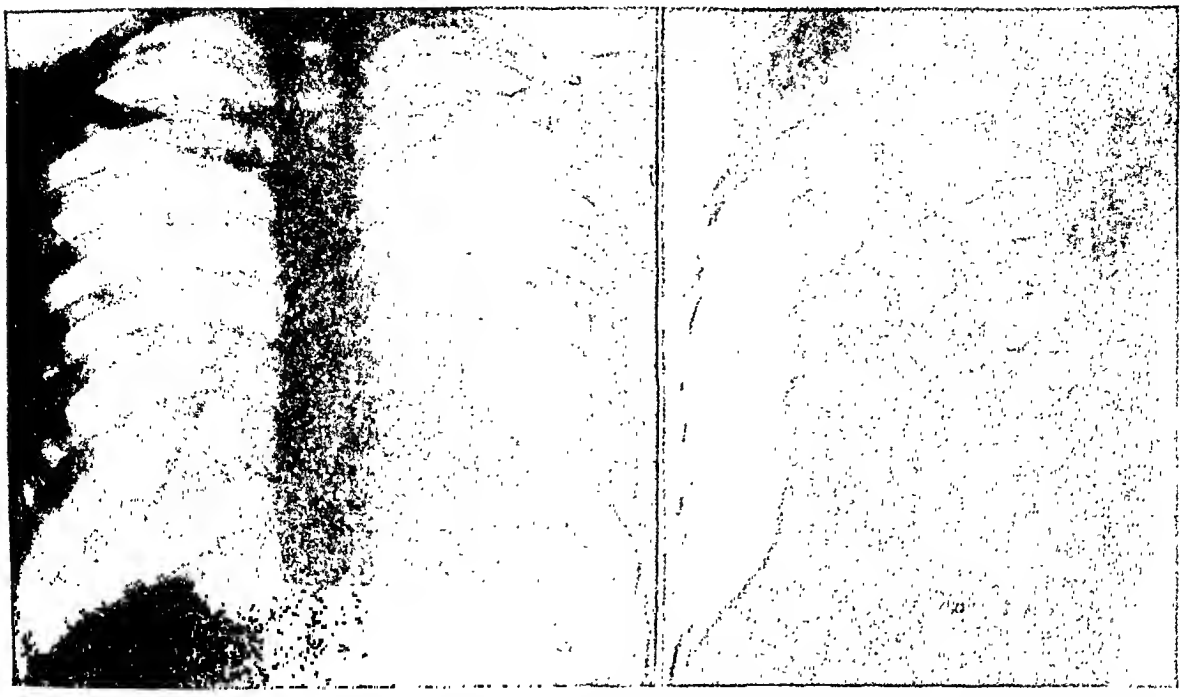

FIG. 5.—Anterior and left oblique teleradiograms in Case 2 with funnel depression. The heart is displaced bodily to the left.

border and the apex beat was the outcome of flattening or compression of the heart within the jaws of the sterno-spinal vice.

Where physical activities had been limited on medical advice, displacement of the apex beat had been accepted as evidence of cardiac enlargement and as one reason for imposing the unjustified restrictions.

The heart murmur. A systolic murmur, heard best at the left edge of the depression, was present in all. It was sometimes moderately loud; in three cases it was short and accompanied by splitting of the first heart sound which formed the chief auscultatory sign. The presence of the murmur had always seemed to add significance to the displaced apex beat and had increased the suspicion that organic heart disease had produced cardiac enlargement. Actually the murmur was of the innocent kind and was situated in mid-systole; it might have been produced by the impact of the heart on the sternal bulge, for the murmur was louder in the cup depression than in the saucer variety.

Radiological findings. The wider application of cardioscopy (radiological examination of the heart) in the investigation of patients suspected of heart disease, has in the meantime tended to confirm rather than remove the invalidism imposed after clinical examination of subjects showing depression of the sternum. This has arisen from a failure to discern that the enlargement of the cardiac silhouette in such cases results from a change in the shape of the heart and not from an alteration in its size.

In the two cases of funnel depression (Fig. 2 and 3) the heart was displaced bodily to the left (Fig. 4 and 5), and without changing the shape or size of the heart shadow in either the anterior or oblique views.

In the eight cases of cup depression (Fig. 6 to 9) there was enlargement of the anterior cardiac silhouette with prominence of the pulmonary arc. The enlargement was moderate in four (Fig. 10 and 11), and slight in the other four (Fig. 12). That such enlargement was apparent and not real was confirmed in the oblique views where the heart shadow was normal in size or sometimes seemed small.

In the six cases of saucer depression (see Fig. 15, p. 169), enlargement of the heart shadow in the anterior view was present but slight (Fig. 13), yet the condition is no less important on that account. Indeed, since some of the other signs of sternal depression are less conspicuous in this variety, the recognition of the effects of saucer depression needs even greater

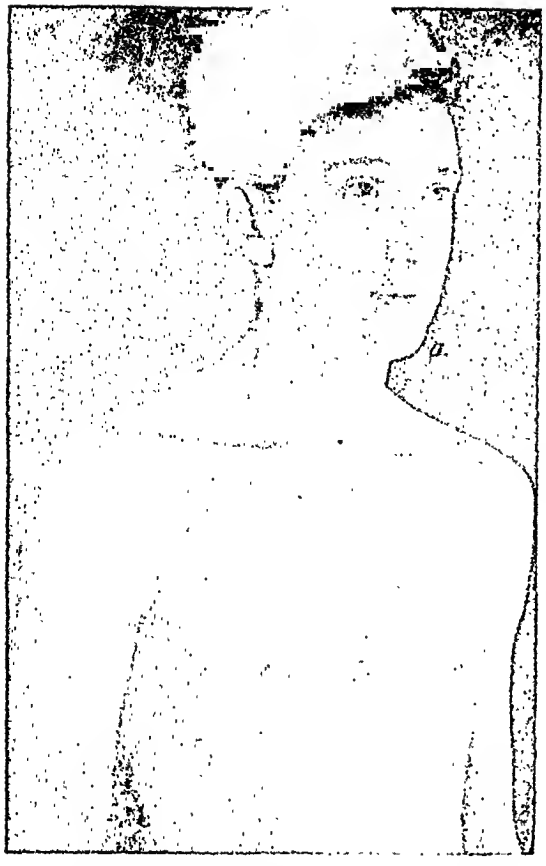

FIG. 6.—Cup depression in Case 4. A–P measurement of 5½ inches against 8 inches in control.

FIG. 7.—Cup depression in Case 5. A–P measurement of 5½ inches against 7½ inches in control.

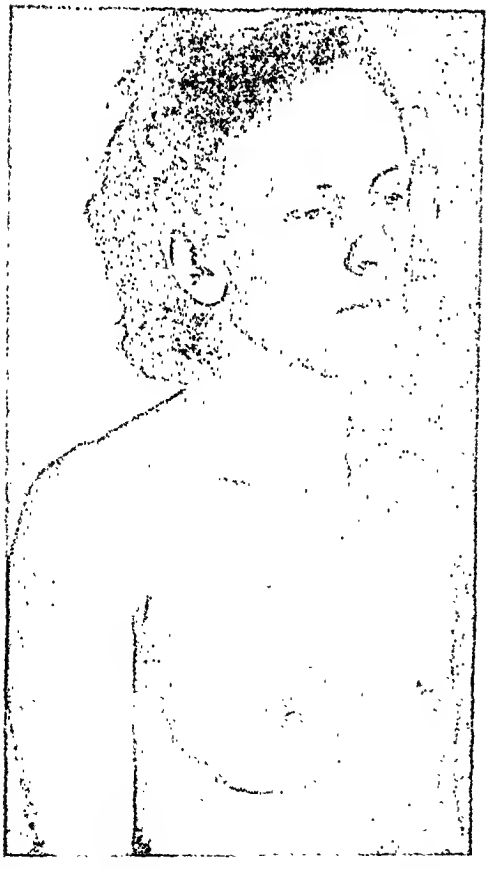

FIG. 8.—Cup depression in Case 6. A–P measurement of 5½ inches against 8½ inches in control.

FIG. 9.—Cup depression in Case 10. A–P measurement of 5¾ inches against 8½ inches in control.

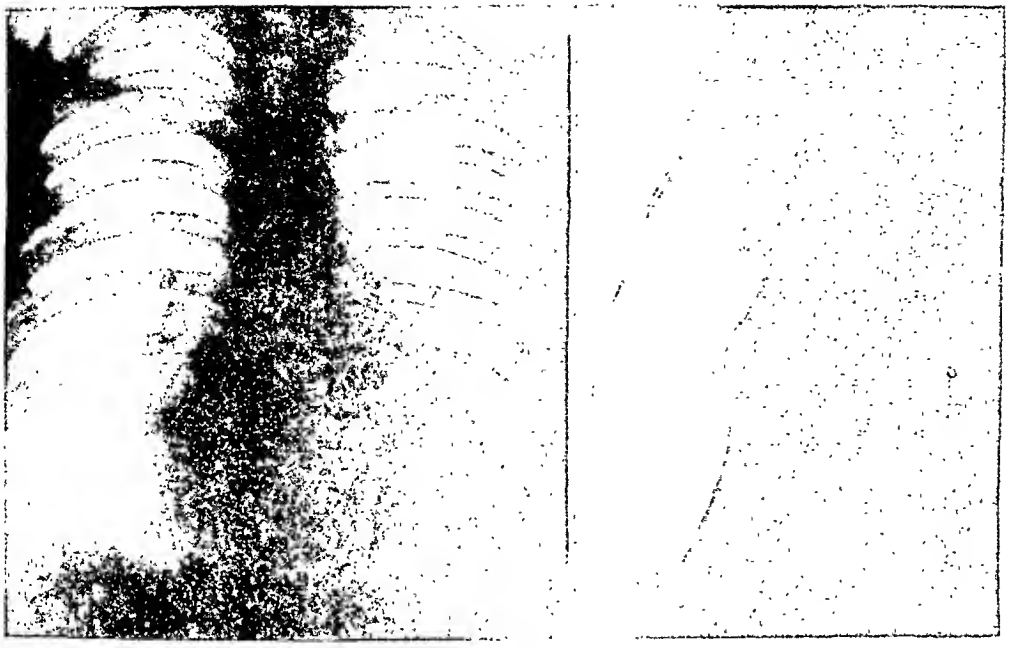

FIG. 10.—Anterior and left oblique teleradiograms in Case 4 with cup depression. The heart shadow is enlarged and the pulmonary arc is prominent in the anterior view, but the heart is normal and moved backwards in the left oblique.

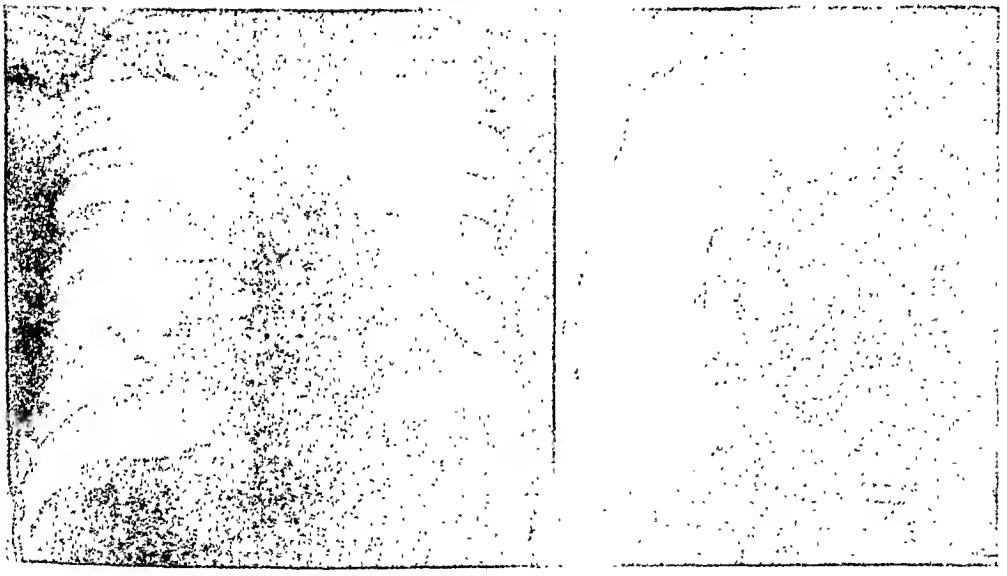

FIG. 11.—Anterior and left oblique teleradiograms in Case 10 with cup depression. The heart shadow is enlarged in the anterior view, but normal and displaced backwards in the left oblique.

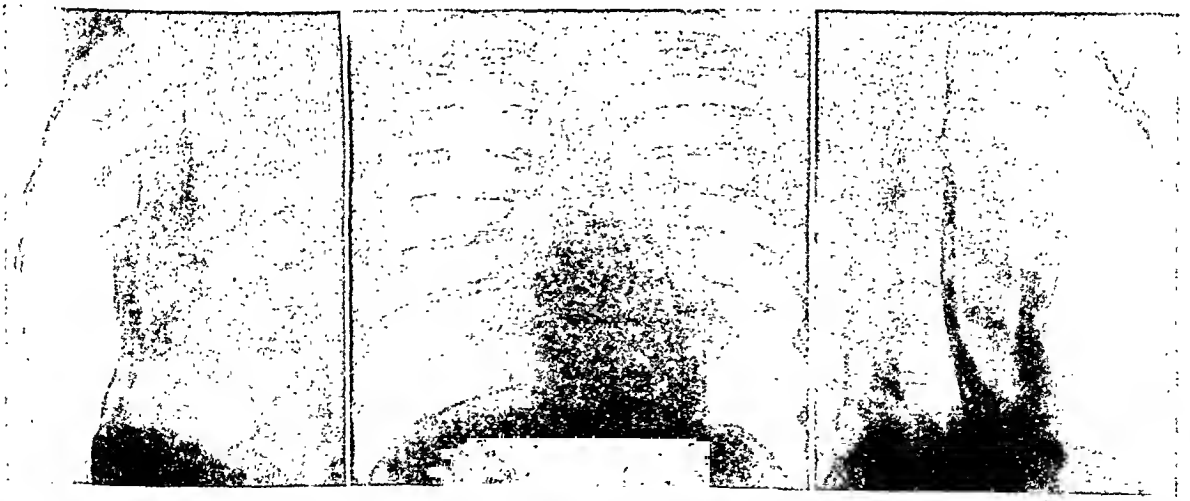

FIG. 12.—Anterior and left and right oblique teleradiograms in Case 5 with cup depression. The heart shadow is moderately enlarged in the anterior view but normal in the obliques.

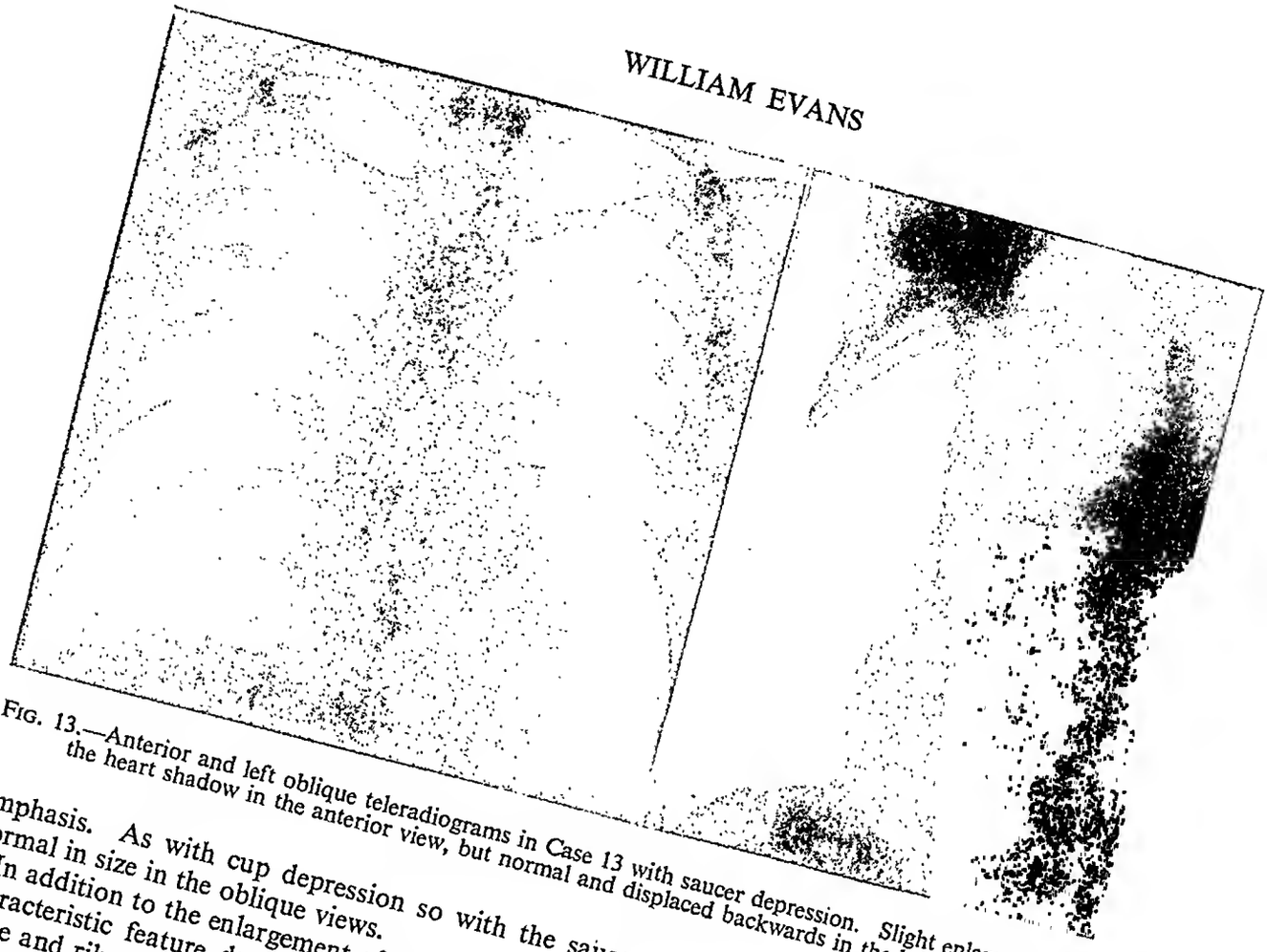

FIG. 13.—Anterior and left oblique teleradiograms in Case 13 with saucer depression. Slight enlargement of the heart shadow in the anterior view, but normal and displaced backwards in the left oblique.

emphasis. As with cup depression so with the saucer variety the heart shadow appeared normal in size in the oblique views.

In addition to the enlargement of the cardiovascular silhouette in the *anterior* view another characteristic feature during cardioscopy was the transparency of the shadow. Thus the spine and ribs were plainly discernible through the heart, and so light was the heart shadow to the right of the sternum that it was sometimes difficult to make out on screening alone the limits of the right border; the right auricle was also often lifted by the sternal depression below causing widening of the right cardiophrenic angle; emphysema was not a factor in the production of such changes. Immediately to the left of the spine a band-like area especially lacked the customary density of the heart shadow in this position. Naturally such transparency was absent in the funnel depression, and was more obvious in the cup depression than in the saucer variety. In the *left* (II) *oblique* position, apart from the size of the heart appearing normal or even smaller, a characteristic finding was its displacement backwards to overlap the adjacent bodies of the vertebræ. Similarly the aortic window (the light area below the aortic arch) was constricted by the approximation of the cardiovascular and spinal shadows, makes it the spine. This trespass on the clear areas provided by the aortic window and the retrocardiac space in this view, caused by the fusion of the cardiovascular and spinal shadows, makes it difficult to identify the separate structures and impoverishes the picture. Such effects were naturally more noticeable in the funnel and cup depression than in the saucer variety. The heart was also normal or narrow in the *right* (I) *oblique* position where the bony deformity in relation to the heart was seen to best advantage. There was no abnormal displacement of the barium-filled œsophagus apart from a slight shift to the left in the two cases with funnel depression.

No significant changes were found in the *electrocardiogram* except that the S wave in lead I was sometimes deep (Fig. 14).

DISCUSSION

Depression of the lower end of the sternum is a common deformity and Lang (1928) found it in 3·5 per cent of children in the first year of schooling. This incidence makes it important to recognize and accept the innocent effects that the deformity may produce on the heart so as to guard against misinterpreting these for the more sinister signs connected

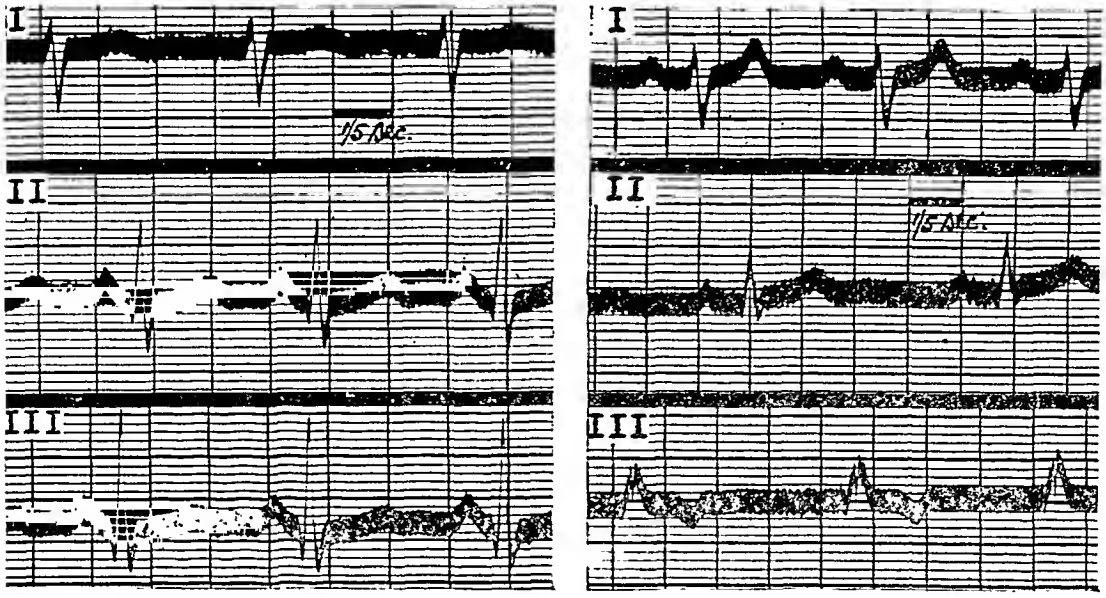

FIG. 14.—The electrocardiogram from Cases 1 and 7 showing deep S wave in lead I.

FIG. 15.—Saucer depression in Case 13. A–P measurement of 6 inches against 7½ inches in control.

with true cardiac enlargement and the conditions that give rise to it. There are many factors said to play a part in the evolution of this sternal deformity, such as abnormal length of the ribs (Flesch, 1873), occupations like cobbling (Laennec, 1819), intra-uterine arrest of the development of the sternum (Ebstein, 1882), and post-natal abnormal development in a child of slender build arising from faulty posture (Kuhns, 1931). Here there was no evidence that any had resulted from congenital maldevelopment, and in all it appeared in early childhood when it might have been the outcome of a disturbance in the mechanism of respiration.

Greatest interest lies with the changes in the heart shadow on cardioscopy. Cardiac hypertrophy was reported by Bein (1912), Frühwald (1913), and Findlay (1921), while Roesler (1943) spoke of circulatory embarrassment. No such effects were observed in my series; the cardiac silhouette was always enlarged in the anterior view in both the cup and saucer depression, but the heart was merely altered in shape and not in size, for it was normal and sometimes small in the oblique views. The explanation of the irregular findings on cardioscopy comes from a study of the thoracic measurements in sternal depression. The antero-posterior measurement of the heart in a series of necropsies on adults was about 3 inches, and the thickness of the sternum, vertebral column, and the soft tissue covering them was about $3\,^3/_4$ inches. Thus when the external antero-posterior measurement of the chest is $6\,^3/_4$ inches the heart assumes its natural contour and is not subject to external pressure.

In 16 subjects serving as control cases for the present series, being of the same age and of comparable build, the external antero-posterior measurement of the chest was never less than 7 inches and the average was 7 3/4 inches. If this measurement, however, is less than 6 1/2 inches in an adult the approximation of the sternum and spine is such as to compress the heart and reduce its antero-posterior measurement, extending its lateral limits and so enlarging the anterior shadow on cardioscopy.

Should enlargement of the heart fail to be explained by disease, it is necessary to entertain a diagnosis of flattening of the heart by sternal depression, and to assess the size of the heart in the left oblique position, observing at the same time its relation to the spine. Confirmation of the condition is readily obtained from the external antero-posterior measurement of the chest. Such measurement for the series (Table I) was never greater than 6 1/4 inches, so that this figure or a lesser one predicts for the subject a widened cardiac silhouette in the anterior view or displacement in the case of funnel depression. For this reason a measuring calliper is an indispensable instrument whenever an opinion is sought on such a radiological appearance of the heart.

Summary and Conclusions

Sixteen adults in whom there was a moderate or greater degree of depression of the sternum were examined especially for its effect on the heart. The association of a displaced apex beat and a systolic murmur with the deformity had led to a restriction of physical activities in every case; this invalidism had been enforced more rigidly whenever radiological examination had been added, because it had shown a big heart shadow. The symptoms were never once the result of heart enlargement or embarrassment, but were the direct outcome of the physical inactivity or mental anxiety resulting from the unwarranted invalidism.

According to the depth of the depression the cases were separated into three groups. Two cases belonged to the first group of *funnel* depression, where the hollowing was deep and the external antero-posterior chest measurement was 4 1/2 and 5 inches respectively. Eight cases belonged to the second group of *cup* depression, where the receission was moderately deep and its apex more rounded; the external antero-posterior chest measurement in these cases varied from 5 1/4 to 5 3/4 inches. Six cases formed the third group of *saucer* depression, where the dip was shallower and wider and the external antero-posterior chest measurement was 6 or 6 1/4 inches.

The radiological findings were characteristic for each group. Thus, in funnel depression the heart was displaced bodily to the left of the spine and was unchanged in shape or in size. In the cup depression the cardiac silhouette in the anterior view was less dense than normal and was moderately enlarged with prominence of the pulmonary arc; in the left oblique view the heart shadow was normal or small, and was displaced backwards to overlap the spine, thereby obliterating the clear areas of the aortic window and the retrocardiac space. Similar effects, although less in degree, were observed in the saucer depression; the importance of this last group lies in the less obvious chest deformity giving rise to changes which may lead to the erroneous interpretation of the enlarged cardiac area seen on radioscopy if the effects of this saucer depression are not known.

It needs final emphasis that none of the 16 cases with depression of the sternum showed actual enlargement of the heart, nor suffered from symptoms related to the heart. Indeed, they were all healthy and were handicapped only by the restrictions imposed on them by a medical examination that had misinterpreted the clinical and radiological signs.

I wish to thank Dr. John Parkinson, Physician to the Cardiac Department of the London Hospital, for his helpful criticism of this paper.

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AMMI VISNAGA IN THE TREATMENT OF THE ANGINAL SYNDROME*

BY

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Received August 28, 1945

The plant *Ammi Visnaga*, known in Arabic as "Khella," grows wild in the Eastern Mediterranean countries and in Arabia. The decoction of its dried seeds is much used by the population and is frequently prescribed by local physicians as a diuretic and antispasmodic in cases of ureteral stones. Of the several crystalline substances isolated from the seeds, quantitatively the most important are a substance called khellin ($C_{14}H_{12}O_5$) and a monoglucoside ($C_{19}H_{20}O_5 2H_2O$). Almost the entire activity of *Ammi Visnaga* is due to the khellin.

Khellin was first prepared in an impure form by Mustapha (1879) and again by Malosse (1881). Fantl and Salim (1930) isolated and purified both khellin and the glucoside; they determined their respective properties and composition, established methods for their separation, and suggested the most likely structural formulæ. The pharmacognosical features of the two substances were studied by Fahmy (1931). The final determination of their structural formulæ was made by Malik (1932) for khellin and by Hassan (1932) for the glucoside, both working under the direction of Prof. R. W. West of Cairo University. In 1934 the decoction and the tincture of *Ammi Visnaga* were included in the Egyptian Pharmacopœia. Pharmacologically the action of khellin was studied by Samaan (1932) who showed that it relaxes all the visceral smooth muscles by direct action on the muscle fibres. Samaan also suggested changing the name of khellin to visamin. We prefer the original name since it is free from the implication of containing an amino group. Preliminary experiments of Anrep and Misrahy (1945) showed that khellin is a strong coronary vasodilator.

The object of the present research was to investigate by physiological methods the action of khellin on the cardiovascular system with special reference to the coronary circulation and the heart muscle, and also to study its action clinically on patients suffering from angina pectoris and coronary thrombosis.

I. Physiological Part

The experiments were made on dogs, using the heart–lung preparation and the whole animal. The coronary blood was collected from the coronary sinus through a Morawitz cannula and the blood flow was registered by means of a small volume recorder. The khellin at our disposal was a crystalline product of a constant melting-point (153° C.). We should like to thank Prof. Samaan for the supply of a small sample of the active material for our preliminary experiments. The rest of the experiments and almost all the clinical observations were made with khellin prepared in the Physiological Laboratory by a modified method of Fantl and Salim. The results of our observations are best presented by a description of a few typical experiments.

Experiments on the Heart–Lung Preparation

Experiment 1. Heart–lung preparation; blood pressure 100 mm. Hg.; cardiac output 500 c.c. per minute; temp. 36·5° C. The coronary sinus outflow was steady at 41–42 c.c. per minute. On administration of 10 mg. of khellin the coronary blood flow rapidly increased to

*A preliminary communication was published in the *Gazette of the Faculty of Medicine*, Cairo, 1945, 13, 39, by Kenawy and Barsoum.

120 c.c. per minute. The blood flow remained increased up to the end of the experiment, over 3 hours, fluctuating between 110 and 130 c.c. per minute. The total amount of blood in the circulation was about 1 litre and the weight of the heart 85 g. The record obtained in this experiment is reproduced in Fig. 1.

Experiment 2. Blood pressure 95 mm. Hg.; cardiac output 450 c.c. per minute; temp. 37° C. The coronary blood flow was steady at 33 c.c. per minute. After administration of 1 mg. of khellin dissolved in 5 c.c. of blood it increased to 50 c.c. per minute; after another 1 mg. it became 70 c.c. per minute. A further administration 10 minutes later of 3 mg. increased the flow to 100 c.c. per minute. The heart rate and the systemic output remained constant while the increase in the coronary circulation was maintained to the end of the experiment. The amount of blood in circulation was about 1 litre and the weight of the heart 74 g. A record of this experiment is given in Fig. 2.

Experiment 3. This experiment was made in order to determine the minimal active dose of

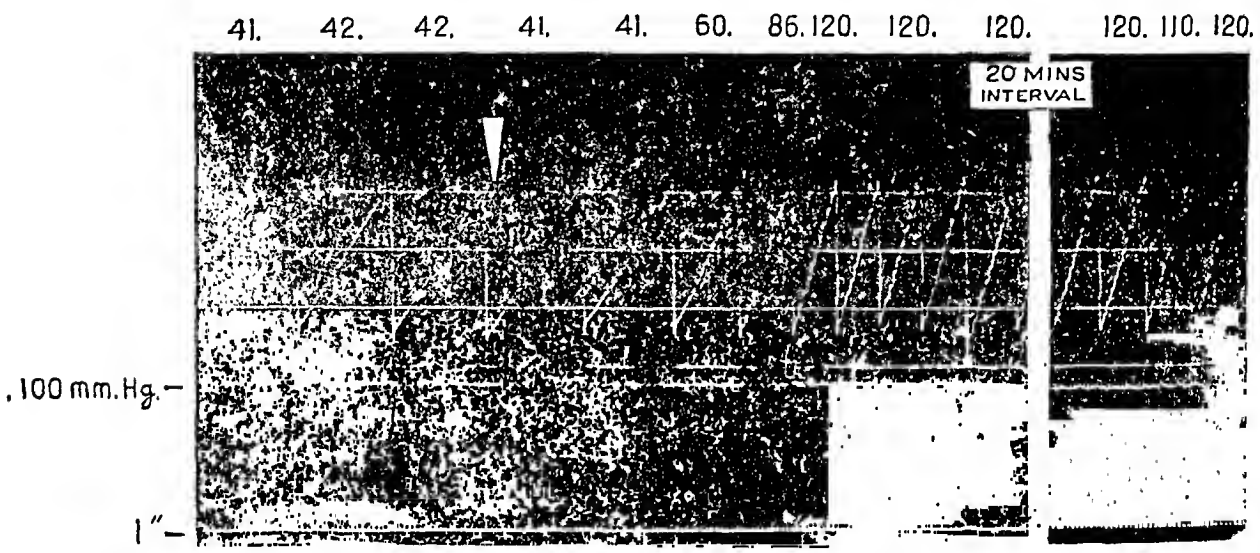

FIG. 1.—*Expt. 1.* Heart-lung preparation. Shows outflow from coronary sinus registered by volume recorder calibrated in 5 c.c. The figures added above the smoked paper give the flow in c.c. per minute. Blood pressure and time in seconds are recorded below. The arrow indicates injection of 10 mg. khellin.

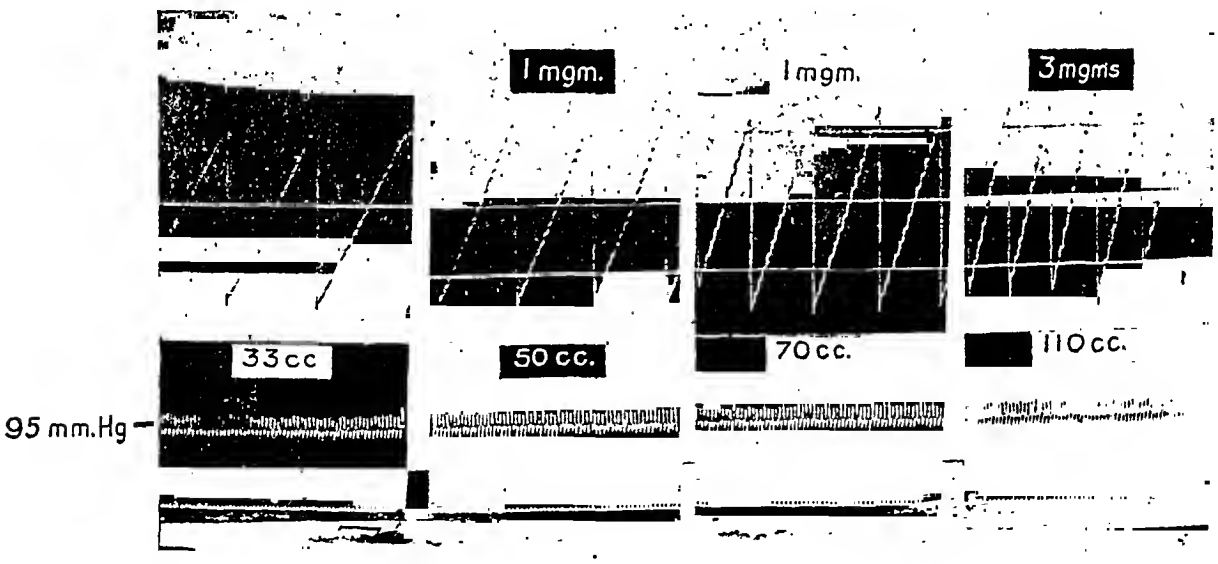

FIG. 2.—*Expt. 2.* Heart-lung preparation. Shows effect of small doses of khellin (upper figures) on coronary flow, registered by volume recorder and given in c.c. per minute in lower figures. The records were taken at intervals of 10 minutes.

khellin that would dilate the coronary blood vessels. The conditions of the experiment were like those of experiments 1 and 2. The amount of blood in circulation was measured as exactly as possible. The khellin was administered in successive small doses at intervals of 5 to 10 minutes.

Mg. of khellin administered	Approximate concentration	Coronary blood flow in c.c. per minute
None	None	44–46
0·4	1 in 2,500,000	47–49
0·4	1 in 1,250,000	56–57
0·8	1 in 625,000	83–85
3·2	1 in 208,000	120–130
3·2	1 in 125,000	160–180

It can be seen from the above and other similar experiments on the dog that the minimal active concentration of khellin in the heart–lung preparation is about 1 in 2,000,000. With concentrations of the order of 1 in 200,000 the coronary blood flow increases 3 to 4 times the initial volume. The action of khellin, although very considerable, is less than that of amyl nitrite, but it has the advantage of being much more prolonged. We should like to add that the isolated perfused rabbit's or cat's heart is not a suitable object for the study of the coronary dilator action of khellin. As with many other substances the results obtained are indefinite and inconclusive.

Samaan (1932) reports that in high concentrations khellin causes a weakening of the isolated perfused frog's and rabbit's heart. In repeated experiments on the heart–lung preparation no such effect was observed. Gradual administration of doses as high as 100 mg. causes no change in the heart volume, which is generally recognized as the best measure of cardiac fitness (Fig. 3). It is, therefore, obvious that doses many times greater than those causing a conspicuous coronary vasodilatation have no injurious effects on the heart muscle. Cardiograms taken before and after administration of khellin were found to be identical in all respects. The pulmonary blood pressure and the rate of the denervated heart were not affected.

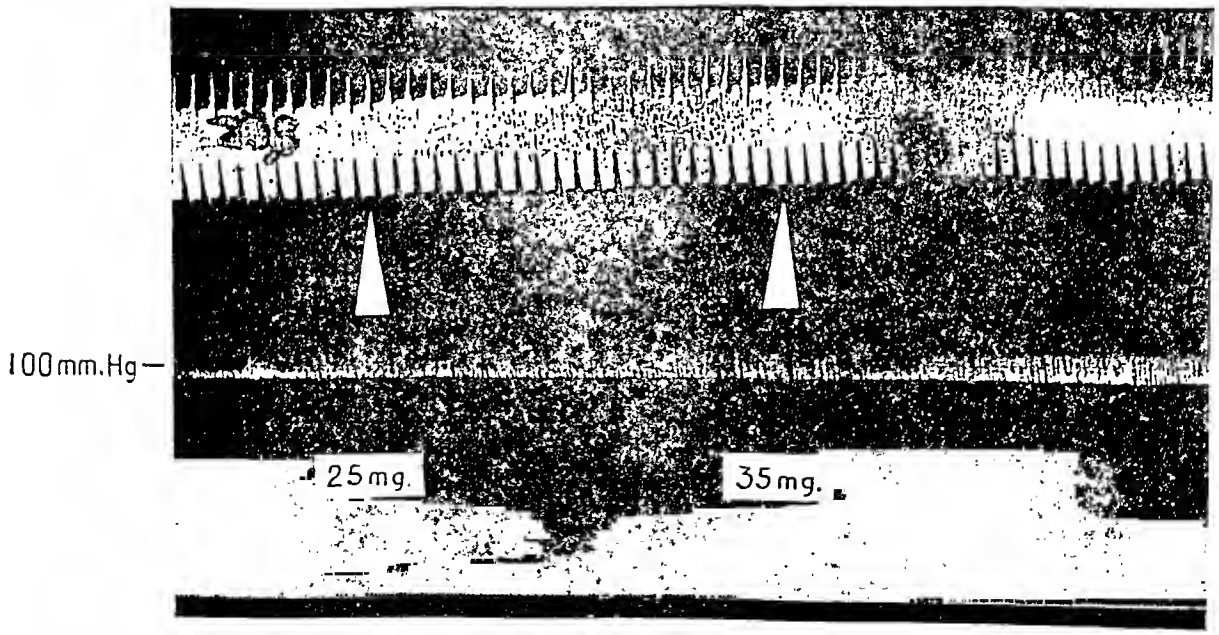

FIG. 3.—Heart–lung preparation. Effect of khellin on the heart volume; 25 and 35 mg. of khellin were administered at first and second arrow respectively.

Experiments on the Whole Animal

According to the observations of Samaan (1932) intravenous injections of khellin into the whole animal lead to a temporary fall of the arterial blood pressure, to a slowing of the heart rate which is vagal in origin, and to some acceleration of the respiration. Our experiments on the whole animal were made on dogs anæsthetized with chloralose (0·075–0·1 g. per kg.) or medinal (0·22 g. per kg.). The blood pressure was measured in the carotid artery while the respiration was recorded by a Marey's tambour which was placed on the sternum. Intravenous injections of khellin produced effects similar to those described by Samaan but only on rapid administration of large doses. Immediately after a rapid injection of 20–30 mg. the blood pressure drops to about 50 mm. Hg., the heart beats considerably slower, and the respiration is momentarily arrested. The entire effect lasts for only a short time; within a minute or two the general blood pressure, heart rate, and respiration return to normal. Slow intravenous injections at the rate of 2 mg. per 20–30 seconds can be continued for a long time without ill effects (Fig. 4). The maximal total dose so injected was 10 mg. per kilogram.

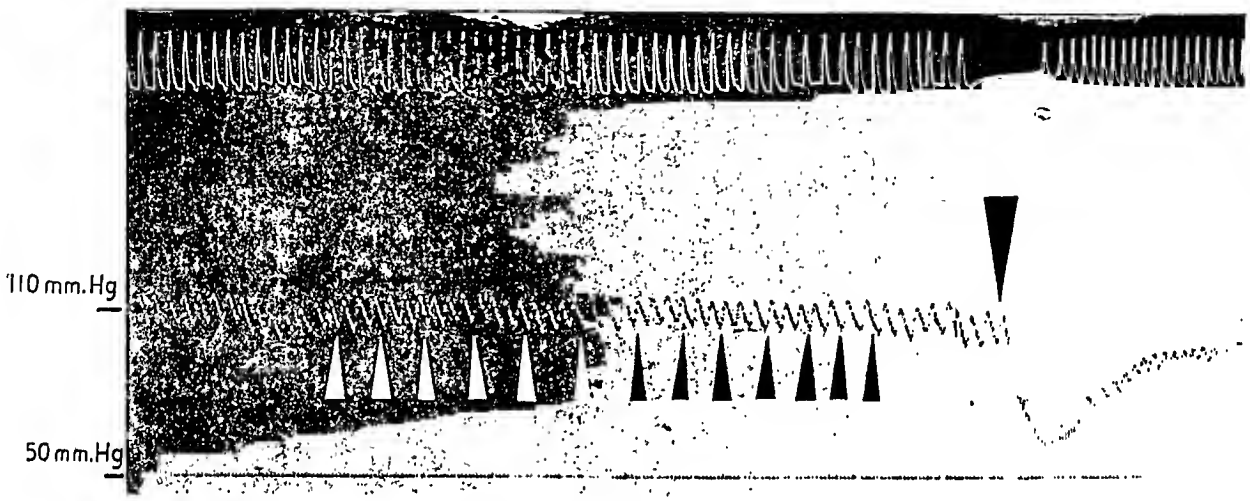

Fig. 4.—Effect of gradual and of rapid intravenous injections of khellin on the blood pressure and respiration of the whole animal. The end of injections of each 2 mg. is marked by an arrow pointing upwards. A rapid injection of 20 mg. was made at the last arrow pointing downwards. Time in seconds, arterial blood pressure, and respiration from below upwards.

It follows from these experiments that subcutaneous and intramuscular injections should be well tolerated. Doses of 40–50 mg. per kilogram cause a prolonged fall of the general blood pressure due to peripheral vasodilatation mainly of the splanchnic area.

The coronary vasodilator action of khellin can be observed not only in the heart–lung preparation but also in the whole animal. Experiment 4 is selected from amongst several to illustrate the effect.

Experiment 4. Dog, 11 kg., anæsthetized with chloralose and injected with chlorazol-fast-pink as anticoagulant. To prevent loss of blood the coronary cannula is connected with the jugular vein. It is opened to the volume recorder only during the measurements of the coronary blood flow. Before administration of khellin the coronary blood flow was steady at 27 c.c. per minute. After injection of 10 mg. the flow increased to 50 c.c. After injection of another 10 mg. the flow reached 80 and then 100 c.c. per minute. The general blood pressure remained unchanged at 105 mm. Hg. Towards the end of the experiment, one hour later, the coronary blood flow was 90 c.c. per minute and the arterial blood pressure, 95 mm. Hg.

Khellin exerts no stimulating effect on the sympathetic nervous system. It is, therefore, unlikely that its coronary vasodilator action is similar in nature to that produced by adrenaline. As with other smooth muscles it acts directly on the muscle fibres of the blood vessels. The apparently selective action of khellin on the coronary blood vessels is due to their much greater sensitivity to the drug as compared with the systemic blood vessels.

II. Clinical Part

As a clinical trial khellin was given to 46 patients of whom 38 had angina pectoris of effort or decubitus or both, and 8 had coronary thrombosis. The cases of angina pectoris were graded as mild, moderate, or severe. Those subject to occasional pain on effort were classed as mild; those with more frequent pain on effort and occasionally apart from it, who used trinitrine regularly, as moderate; those with frequent pain on slight effort or at rest and especially at night, who used trinitrine freely, as severe. On this basis, 8 cases were mild, 17 moderate, and 13 severe. There were 34 men and 4 women, and their ages ranged from 35 to 66 years. The duration of anginal symptoms was 3–12 years in 14 cases, 1–2 years in 17, and less than a year in 7. Hypertension was present in 15 cases and diabetes in 7. The Wassermann reaction was negative in all but one case. Abnormal electrocardiograms were recorded in 17 cases, and enlargement of the heart and aorta was found in 4 cases. Of the 8 cases of coronary thrombosis, 6 had recurrent attacks of pain, and 2 had dyspnœa during the period of complete rest following the onset of symptoms.

The subjective effects of the drug were recorded in each case. In some, electrocardiographic changes provoked by graded exercise were recorded before and after treatment. Exercise tolerance tests were performed whenever the patient's condition permitted. As a control, injections free from khellin or containing a much reduced dose were substituted without the patient's knowledge.

Method of Administration and Dosage. The following preparations were tried.

1. Purified liquid extract containing 40 mg. of active principle per c.c.; dose 30–60 minims in water with meals.
2. Pills each containing 25 mg.; dose 2–3 pills thrice daily after food.
3. Solution of 60 mg. per c.c. by intramuscular injection; dose 1–2 c.c. daily or on alternate days, and for the treatment of individual attacks.

Doses of 10–30 mg. per day by injection were tried first and found to be ineffective. A dose of 60 mg. a day gave encouraging results; and 90–120 mg. a day still better. Single doses of 150–200 mg. were given to healthy volunteers without ill effect. An average effective dose proved to be 90 mg. a day. The injections caused slight and transient local pain. The average oral dose was 40 mg. thrice daily.

Anginal Group

The response to khellin was arbitrarily classed as good, moderate, or negative; good when the anginal attacks ceased altogether or became very infrequent and mild, moderate when they diminished in frequency and severity, and negative otherwise. On this basis the results are summarized in Table I. The duration of observation and treatment varied from 3–9 months, being 6 months or longer in half, excluding those classed as failures where treatment was abandoned earlier.

TABLE I

Grade of Anginal Pain	Response to Treatment		
	Good	Moderate	Negative
Mild	7	1	—
Moderate ..	15	1	1
Severe	6	5	2
Total ..	28	7	3

Continuous Treatment. Oral administration of the liquid extract or pills alone was tried in 13 cases, intramuscular injections alone in 9, and both methods combined in 16. The 13 cases treated by oral doses of 120 mg. of khellin a day all showed a good response. Given

by mouth, the drug required 1–3 days to reach its full effect. The severity of the attacks was reduced before the frequency. If the drug was discontinued for a few days the attacks reappeared, sometimes in milder form.

Of 9 cases treated by injections alone, in doses of 90 mg. daily or 120 mg. on alternate days, 8 showed a good response. On cessation of the injections, or on substitution of inert injections as a control, the anginal attacks recurred, and restarting the injections again resulted in relief. The effect of each injection appeared to last 24–36 hours.

The 16 patients treated by a combination of oral and intramuscular khellin were mostly classed as severe cases. The injections and oral doses were given on alternate days. This combined treatment seemed more effective in severe cases, though two so treated failed to respond. One of these also had carcinoma of the stomach, and the other, after several days of frequent anginal attacks, died suddenly from coronary thrombosis. The third failure was treated orally for three weeks without effect.

Treatment of Individual Attacks. Patients were given liquid extract of khellin to take in the attacks, and nearly all reported favourably, especially in the case of more prolonged attacks of pain occurring apart from effort. In a few cases, we had the opportunity of giving injections during an attack and relief followed within a few minutes, rather more slowly than after trinitrine tablets.

Objective Tests. In some cases electrocardiograms before and after a standard exercise test of stepping on a chair 40 cm. high at a rate of 30 times a minute were recorded. Later,

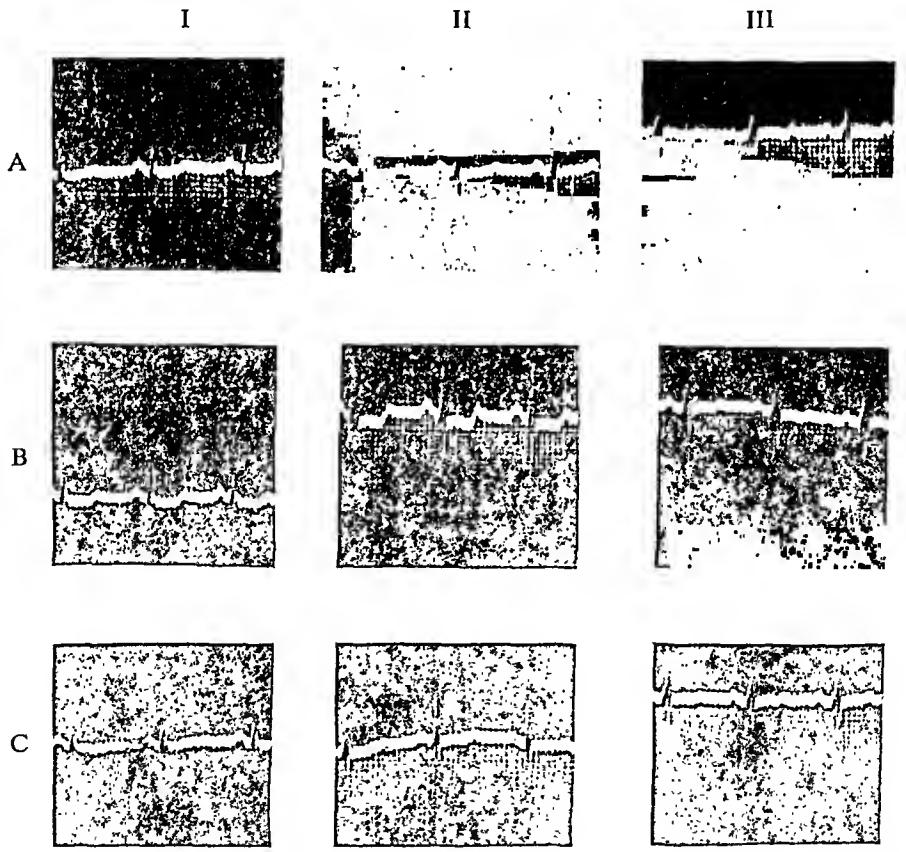

FIG. 5.—Effect of khellin on the electrocardiogram taken after standard exercise. (A) at rest; (B) after exercise; (C) taken on the following day, after a similar exercise, and 30 minutes after an intramuscular injection of 90 mg. of khellin.

the same exercise was performed 30 minutes after an injection of khellin, and the cardiogram was again recorded. Four cases showed S–T depression after a test exercise; in three of these, an injection of 90 mg. of khellin prevented the occurrence of S–T depression after the same exercise (Fig. 5), and in the fourth S–T depression was less conspicuous. In all patients tested, the exercise tolerance, as measured by the exercise described, increased after khellin.

Side Effects. A few patients complained of insomnia after the first few doses, one complained of pain and fullness in the head, and two of dyspepsia after oral administration. The blood pressure, pulse rate, and respiration were unaffected by doses up to 120 mg. of khellin. The clotting time and bleeding time were also unaffected.

Coronary Thrombosis Group

Khellin was given orally or by injection in doses of 90–120 mg. daily for 2–5 weeks after the onset of coronary thrombosis in 8 cases, in 6 of which there were recurrent anginal attacks during the period of recumbency. The drug was also given with morphine at the onset of symptoms. It was well tolerated and as far as could be judged it relieved the spasmodic anginal attacks that followed the initial attack of pain. The variability of the symptoms after coronary thrombosis makes it difficult to assess the effect of drug treatment, and the small number of cases yet treated is insufficient to warrant any definite conclusions as to the value of the treatment. It seems rational to give a coronary vasodilator that does not lower general blood pressure or affect the heart rate, with a view to preventing any associated coronary vasoconstriction, and thus minimizing the area of cardiac infarction.

Conclusions

Physiological experiments show that khellin is an effective coronary vasodilator in doses insufficient to cause any general fall in blood pressure. A preliminary clinical trial has shown that the drug may be given safely and without toxic effects in the doses prescribed. Khellin has advantages over the nitrites and other reputed vasodilators in that it has a selective action on the coronary vessels, and effective doses need not, therefore, lower systemic blood pressure. Its action is slower but more prolonged than that of the nitrites. It may be given in the form of continuous treatment to abolish or reduce the frequency and severity of anginal attacks, or to relieve individual severe attacks of pain. It is no simple matter to assess the value of a drug in the continuous treatment of angina pectoris, as Evans and Hoyle (1933) have shown, for they found that even a placebo might produce subjective improvement in a surprisingly large proportion of cases. This preliminary clinical trial, following physiological experiments, seems sufficiently favourable to justify a further and more extensive therapeutic test of khellin in angina pectoris and coronary occlusion.

Summary

Khellin, the active principle of *Ammi Visnaga*, has been tested physiologically in dogs, both on the heart–lung preparation and on the whole animal, in regard to its effect on the heart and coronary circulation. It was found to be an effective vasodilator with a selective action on the coronary vessels, so that coronary flow was increased by doses insufficient to lower the general blood pressure.

A clinical trial of khellin in 38 cases of angina pectoris and in 8 cases of coronary thrombosis is reported. Continuous treatment, by the oral or intramuscular routes or by both combined, gave favourable results in 35 out of 38 cases of angina pectoris. The drug was given continuously for several weeks to eight patients after coronary thrombosis and appeared to act favourably, but no definite conclusions could be reached as to its value in this respect.

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PREMATURE SYSTOLES ORIGINATING IN THE SINO-AURICULAR NODE

BY

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Received July 15, 1946

Premature systoles arising in the sino-auricular node are characterized in the electrocardiogram by premature P waves that are identical in contour with other sinus P waves and by the absence of a prolongation of the returning cycle. Actually the returning cycle may be shorter than the normal cycle because of prolonged sino-auricular conduction of the premature beat (Wenckebach, 1908). According to Wenckebach and Winterberg (1927) slight changes in contour of the premature P wave do not rule out sinus origin of the premature impulse; these aberrant P waves are ascribed to aberrant conduction in the auricles. Varying intra-auricular conduction has also been suggested (Scherf, 1945) to explain the altered contour of the sinus P wave that occurs in second degree auriculo-ventricular block, accompanied by shortening of the P–P intervals, in those P–P intervals containing a ventricular complex. It would appear that a contour of the premature P wave identical with that of the sinus P wave should be postulated for the diagnosis of sinus premature systoles in order to avoid confusion with auricular premature systoles. In exceptional cases, however, a diagnosis of sinus premature systoles seems justified in spite of a slightly different P wave contour when sinus arrhythmia is absent and when the returning cycle is equal to or shorter than the normal cycle. Because of their rarity, two more cases are being added in this paper to the few instances of sinus premature systoles reported (Wenckebach, 1908; Lewis, 1925; Clerc *et al.*, 1938; Simon and Langendorf, 1944; and Geiger and Goerner, 1945).

Case 1. A man, aged 60, was admitted to the hospital because of neurological complaints. A cardiogram (Fig. 1) was taken to determine the nature of his irregular heart action. The patient had received no medication. Lead I shows an undisturbed regular sinus rhythm with a P–P interval of 0·98 sec.; all the other leads show bigeminal rhythm with a P–P interval of 0·98 sec. alternating with a P–P interval of 0·80 sec. There is a first degree A-V block (P–R equals 0·30 sec.) with variations in the P–R (0·32 and 0·34 sec.) in the leads with bigeminal rhythm. The P waves show only minute differences in contour. The absence of a compensatory pause (the P–P interval in lead I equals the post-extrasystolic P–P intervals in the other leads) identifies the premature systoles as arising in the sino-auricular node. Comparison of lead I with the other leads permits exclusion of other possibilities to be considered in cases of persistent sinus bigeminy, such as non-conducted sinus premature systoles occurring after every second beat, 3 : 2 S-A block with the Wenckebach phenomenon, and alternans of the S-A conduction time.

Case 2. A woman, aged 80, having hypertensive cardiovascular disease, was admitted with a provisional diagnosis of a recent myocardial infarct. No drugs were administered. The cardiogram is shown in Fig. 2. The first seven beats in lead I are regularly spaced and have a P–P interval of 0·64 sec. They are followed by a bigeminal rhythm throughout the rest of the record except for one occasion in lead CF_2. A P–P interval of 0·64 sec. alternates with a P–P interval of 0·70 sec. However, the P wave of the premature beat shows minute differences in contour and might suggest ectopic rather than sinus origin. The first seven beats in lead I have to be considered as a run of premature systoles. This case illustrates the difficulty of distinguishing between sinus premature systoles and

* Aided by the Emil and Fanny Wedeles Fund for Cardiovascular Research. The department is supported in part by the Michael Reese Research Foundation.

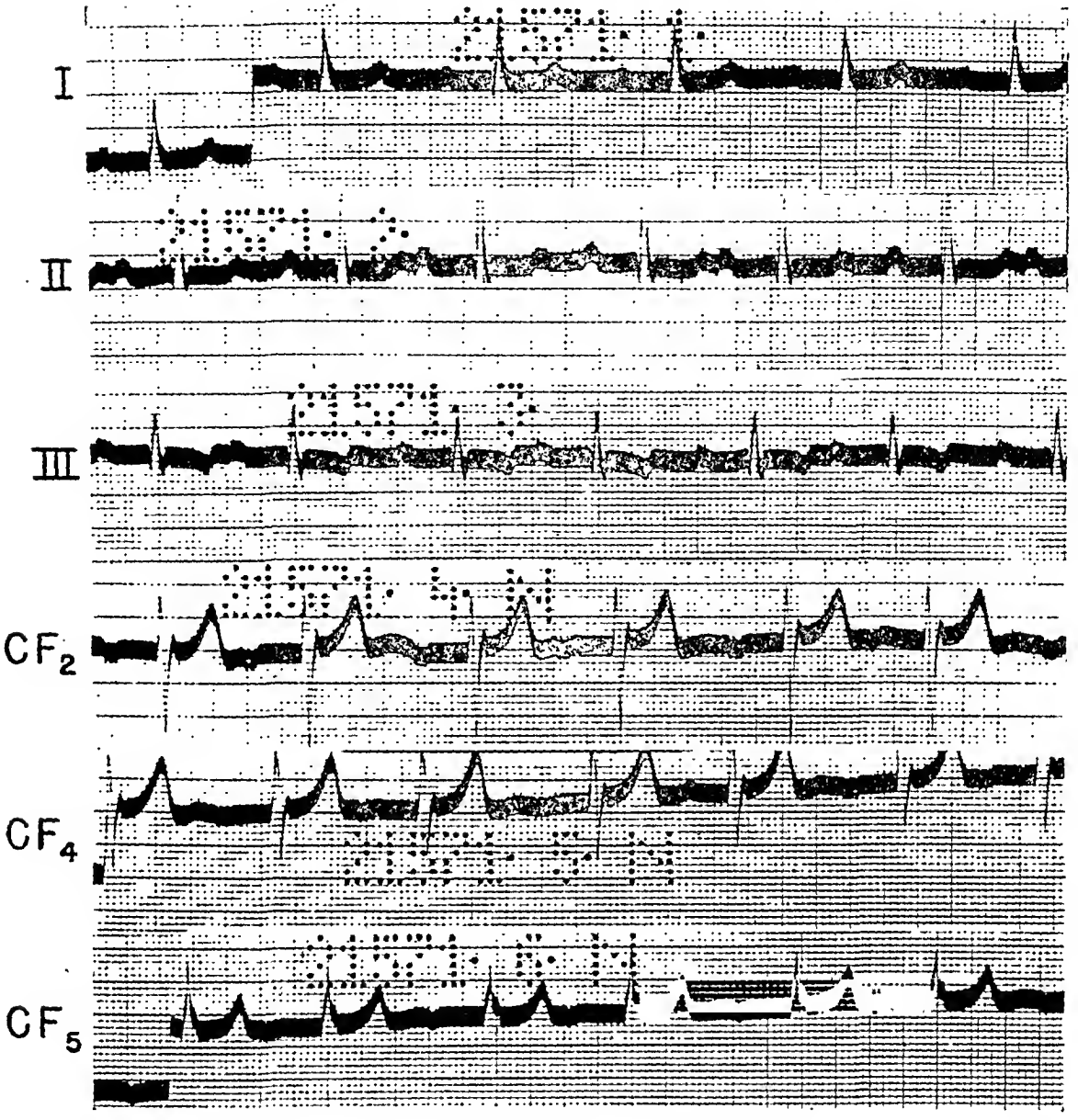

FIG. 1.—Premature systoles originating in the S-A node.

auricular premature systoles arising close to the sino-auricular node. The diagnosis is based in this case upon the close similarity of the premature P waves to the sinus P waves and is made despite the inability to compare the post-extrasystolic pauses with the sinus P–P interval.

SUMMARY

The criteria of electrocardiographic diagnosis of premature systoles arising in the sino-auricular node are discussed and two new cases are described.

The diagnosis is made in spite of slight variations in the contour between the sinus P wave and the premature P wave. In Case 1 the diagnosis is based on the finding of a returning cycle equal to the interval between two sinus P waves in another lead without premature beats. In Case 2 the occurrence of bigeminal rhythm speaks against the diagnosis of simple sinus arrhythmia and favours the diagnosis of premature beats of sino-auricular origin because of the close similarity of the premature P waves to the sinus P waves; however, the diagnosis of auricular premature systoles arising from a focus close to the sinus node cannot be ruled out.

We are indebted to Dr. L. N. Katz for his criticism and aid in preparing this paper.

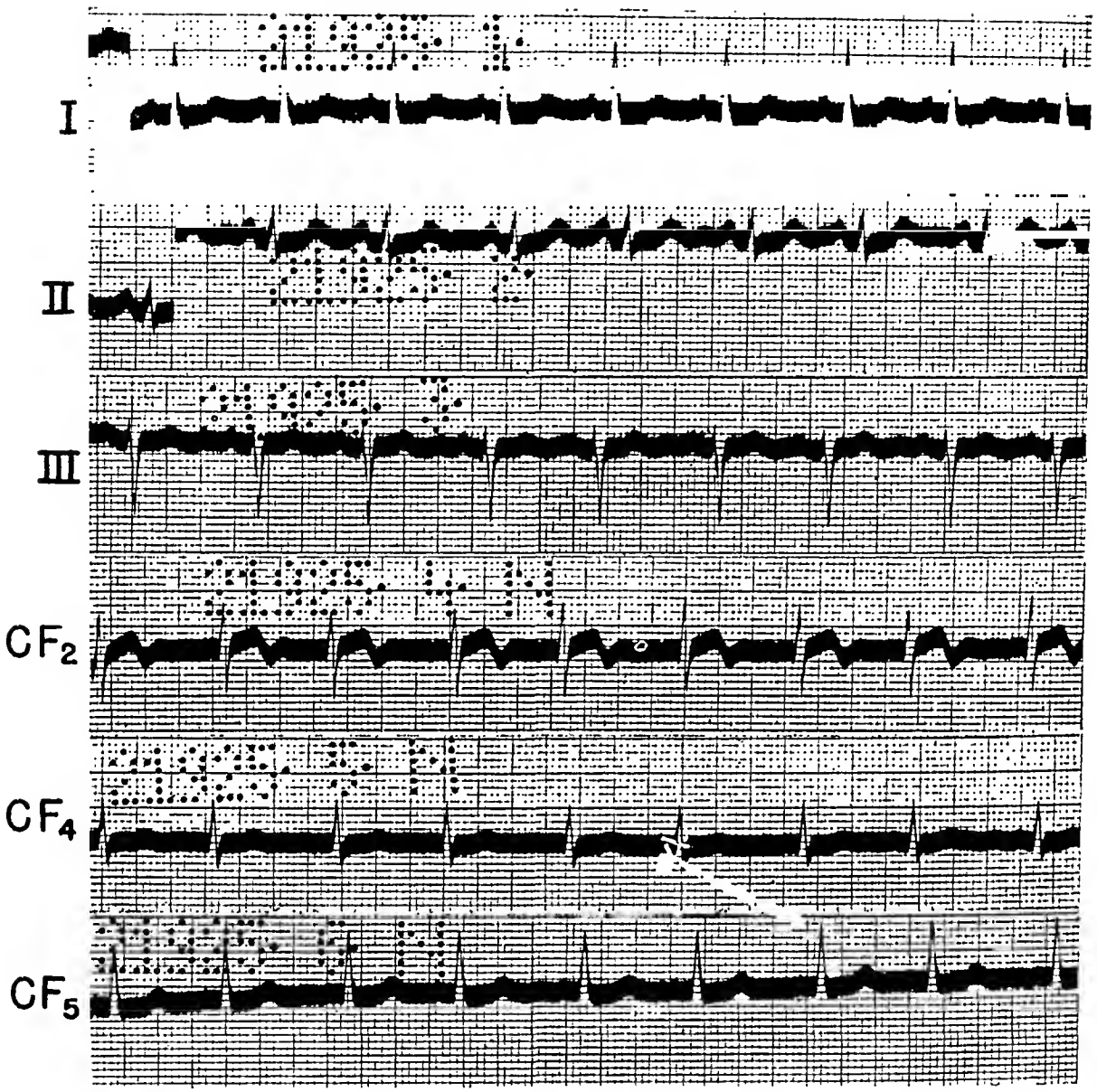

FIG. 2.—Premature systoles originating in the S-A node.

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DISSECTING ANEURYSM OF THE AORTA, WITH CARDIOGRAMS SUGGESTIVE OF CARDIAC INFARCTION

BY

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Received May 16, 1946

Two cases are here described in which the clinical picture was in some respects similar to that of myocardial infarction, and the electrocardiographic changes, although atypical, also suggested this diagnosis. Post-mortem examination showed the presence in each case of a dissecting aneurysm of the aorta, but revealed no evidence of any coronary infarction past or present.

The clinical pictures were suggestive of myocardial infarction in several respects. In each the pain was as severe as that seen in many cases of cardiac infarct, and its position although not typical was compatible with this diagnosis. In Case 1, the pain started in the front of the chest and was transmitted to the back; it also radiated to the upper abdomen. In Case 2, the pain was felt in the neck and through to the back under the scapulæ.

Shortness of breath was not a feature in either case, and was not complained of, apart from the distress naturally present before death. But shortness of breath is by no means constant in all cases of coronary infarction. Shock was a marked feature in both patients at some time; in Case 1 the systolic blood pressure fell to 80, and in Case 2 to 90 mm. In Case 2, pericardial friction developed and was sufficiently loud and characteristic to be demonstrated to students, although it was transient. In Case 1 the cardiogram was very suggestive of posterior infarct, and in Case 2 not only was well-marked S–T deviation present in leads II and IV, but the character of the tracing changed rapidly in two days, after which interval a bundle branch block had appeared.

It is interesting to speculate how these changes might have been produced; tabulation of various possibilities may be useful at this stage, to draw attention to these points in the details of the case reports.

1. Myocardial infarction might doubtless co-exist with a dissecting aneurysm.
2. The infiltration of the blood in the middle coat of the aorta might extend to a point where it influenced the coronary vessels passing through the aorta.
3. The infiltrating blood, in its way around the aortic curve, might stiffen the aorta, changing its normal tensions.
4. A similar process might twist it in the same way as the vessel is sometime twisted in pneumothorax, where cardiographic changes are also known to occur (Master, Dacks, Kalter, and Jaffe, 1937).
5. Finally, the ætiology of dissecting aneurysm is sometimes uncertain, but it seems that some degeneration of the substance of the aortic media may be a causative factor. It is theoretically possible that this degeneration may be acute, and may occur simultaneously in the substance of the heart muscle.

First Case Report

Case 1. A woman, aged 62, was admitted to hospital on 29/8/44 for diabetic symptoms with a six months' history of thirst, polyuria, loss of weight, undue fatigue, and paræsthesiæ in hands and feet. She also gave a history of an attack of very severe epigastric pain after a meal one week before admission; this pain radiated to the back, and was thought to be due to a flatulent dyspepsia although there was no such previous history.

Examination showed signs of recent loss of weight although the patient was still obese. Temperature, pulse, and respiration were normal. The retinal arteries were thickened, but the discs and retinæ were otherwise normal.

FIG. 1.—The left ventricle is enlarged. The aortic arch is enlarged and elongated, and projects unusually towards the left apical region. Pulsation was absent on screening.

There was a ringing aortic second sound. There was no clinical evidence of a mediastinal syndrome to suggest aneurysm. The B.P. was 220/120. The upper limbs were normal although the patient complained of tinglings in the fingers. The tendon reflexes were present and there was no sensory loss. The knee and ankle jerks were absent in both legs, and there was diminished sensation to pinprick, and impaired sensibility to light touch. Kinæsthetic sensation was present. The plantar reflexes were flexor.

In the urine (sp. gr. 1028), Benedict's solution was reduced to orange and Rothera's and Gerhardt's tests were positive. The fasting blood sugar was 278 mg. per 100 c.c. Sugar tolerance curve was typical of diabetes with blood sugar of 362 mg. per 100 c.c. two hours after 50 g. of glucose. Blood urea normal. Blood W.R. and Kahn negative. The cerebrospinal fluid was normal, and the W.R. negative.

X-ray of chest (Fig. 1) showed enlargement of left ventricle, aorta unfolded and elongated, with dilatation of the arch. No aortic pulsation. Lung fields clear. A diagnosis of diabetes mellitus with mild peripheral neuritis was made.

The diabetes was controlled by diet and 8 units of insulin b.i.d. and the fasting blood sugar was thus reduced to 120 mg. per 100 c.c.

On 2/9/44 (4 days after admission) the patient asked for a bed-pan and while on the pan complained of sudden intense tearing pain in the upper abdomen and middle of chest radiating to the back. She collapsed and became semi-comatose, with Cheyne-Stokes respiration. On examination she was very cold and the blood pressure fell to 80 systolic, the diastolic reading being unobtainable. Morphia was given with some relief of pain. After a few hours she made a gradual recovery, although the pain in the back persisted for the next two or three days, by which time she also had some difficulty in swallowing. A cardiogram taken 12 hours after the attack showed no changes suggestive of a coronary thrombosis (Fig. 2A).

On this history, especially the persistent pain in the back and the absence of the cardiographic changes of coronary thrombosis, a diagnosis of dissecting aneurysm of the aorta was made. During the next five days the patient's condition improved, the blood pressure gradually rose to 140/80, and the dysphagia disappeared. A further cardiogram (Fig. 2B) taken on 27/9/44 (five days after the attack) strongly suggested a posterior myocardial infarction as shown by a deep Q III and elevated S–T and inverted T, both in lead III. It was then thought that the original diagnosis of dissecting aneurysm was wrong and that a coronary thrombosis must be the cause of the pain and collapse. A further cardiogram (Fig. 2C) still suggested myocardial infarction.

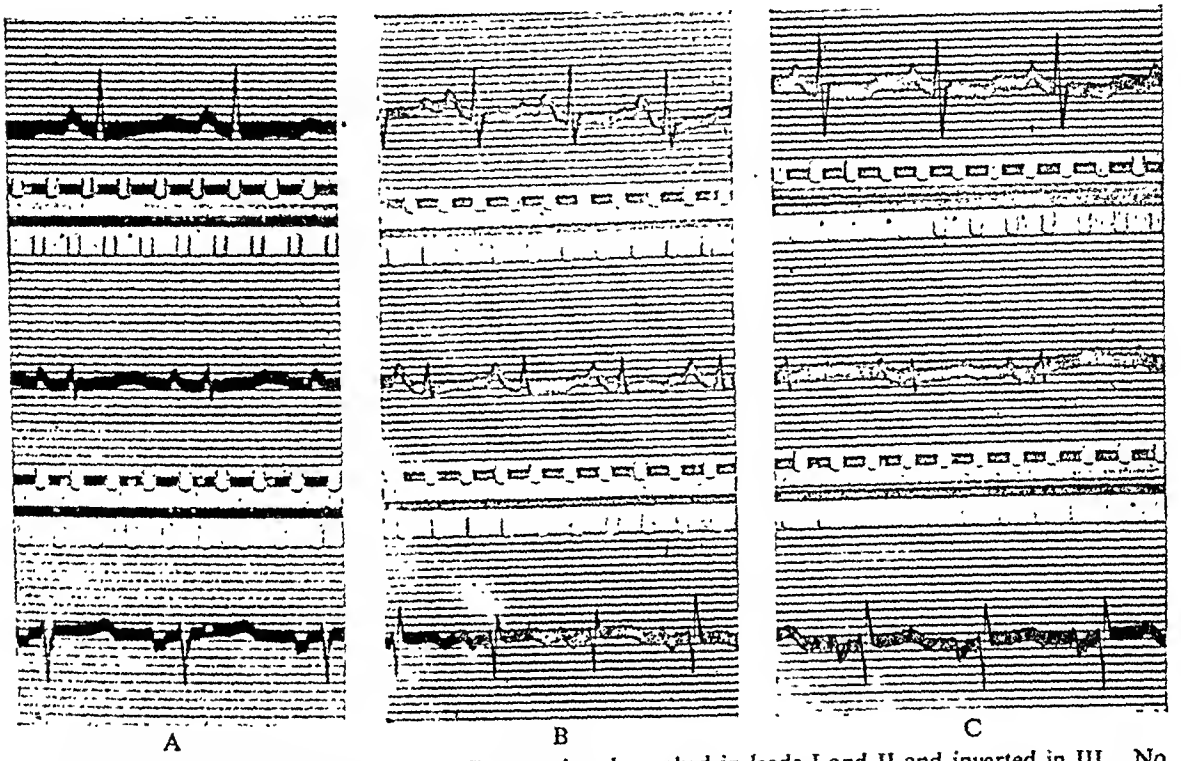


FIG. 2.—Left axis deviation. (A) 2/9/44. P wave sharply peaked in leads I and II and inverted in III. No evidence of myocardial infarct.
(B) 27/9/44. S–T deviation downwards in leads I and II and upwards in III. Deep Q in lead III. T now inverted in lead III.
(C) 11/10/44. Similar to Fig. 2 (B). T wave further inverted in lead I.

On 14/10/44 the patient suddenly had a severe hæmoptysis; she collapsed and rapidly became comatose, the blood pressure falling to 60 systolic. She remained comatose for about three hours and during this time passed a tarry stool and then died. In view of the terminal hæmoptysis and melæna, the original diagnosis of dissecting aneurysm of the aorta was thought to be established, although this made the cardiographic changes difficult to explain.

Post-mortem Examination

Pleural spaces dry, lungs expanded, two large thoracic dissecting aneurysms, loaded abdominal fat depots, small intestine distended with blood.

Heart and Aorta. Heart: 280 g., valves and chambers normal, coronary arteries atheromatous but nowhere occluded or grossly narrowed. Aorta: ectasia and fatty atheroma of ascending portion, severe calcified atheroma of arch and descending thoracic and abdominal portions. Junction of transverse and descending aorta marked by beginning of a dissecting aneurysm localized to medial wall and bulging into subepicardial portion of left lung (8 cm. long, 4 cm. wide, 3 cm. outward bulge into lung) (Fig. 3). No obvious primary intimal tear; instead there was a large patch proximally of ulcerated intima covered by laminated clot. Externally, this part of aneurysm was firmly attached to the lung by fibrous adhesions and organized thrombus. It contained a small linear longitudinal external tear through which a probe passed from the aortic lumen direct into upper lobe of left lung, which was torn up by

FIG. 3.—Posterior aspect of thoracic aorta showing the upper aneurysm with laminated clot at its apex, and the intimal tear of the lower aneurysm.

FIG. 4.—Transverse section of the lower thoracic aneurysm showing compression of the oesophagus. Blood can be seen in the sectioned bronchi of both lungs.

hæmorrhage. 10 cm. distal to the isthmus the intima presented a transverse rupture of 1 cm. (Fig. 3) leading into the proximal portion of a second large dissecting aneurysm, bulging anteriorly and laterally into lower lobe of right lung (8 cm. long, 4 cm. wide, 5 cm. bulge). This was firmly adherent to the lung, and there was no external tear. The left auricle was pushed forwards and the œsophagus compressed anteriorly and to the right (Fig. 4). Blood clot in both aneurysms was lying inside the split medial coat of the aorta. Transverse sections of the abdominal aorta showed two separate incipient aneurysms in the form of hæmatomas of the media (each about 1 cm. in diameter) lying 5 and 9 cm. distal to the coeliac axis (Fig. 5). The overlying intima was intact.

The trachea and bronchi and their branches in both lungs were filled with blood. Lung parenchyma: mixed hæmorrhage and emphysema. Pool of blood in nasopharynx. Stomach: distended with 500 c.c. mixed blood and gastric juice; no peptic ulceration. Intestines: contained blood and tarry material down to rectum. Viscera pale; arteries atherosclerotic.

Death was due to hæmorrhage from rupture of an aortic dissecting aneurysm into the left lung. Blood had entered the air-passages (precipitating an acute emphysema) welled up into nasopharynx and passed down into stomach during patient's terminal coma.

Microscopic Findings. Aorta shows atrophy and diminution in number of medial elastic fibres, fatty degeneration of internal elastic lamina, localized complete medial atrophy underlying some intimal atheromatous plaques, no mucoid or cystic degeneration but marked increase in hyaline and collagen at junction of outer and middle thirds of media (surrounding most internal branches of vasa vasorum) (Fig. 6). It is this part of the middle coat that is split to enclose the hæmatomas and aneurysms. The plane of cleavage in the upper aneurysm is filled with young granulation tissue rich in phagocytes loaded with blood pigment (Fig. 7). The local adventitia shows vasa vasorum cuffed with lymphocytes, histiocytes, and pigment phagocytes. No syphilitic mesaortitis. The upper aneurysm appeared to be the oldest lesion; the outer wall consisted of fibrosing granulation tissue rich in hæmosiderin.

FIG. 5.—Transverse sections of the medial hæmatomas (incipient aneurysms) in the abdominal aorta.

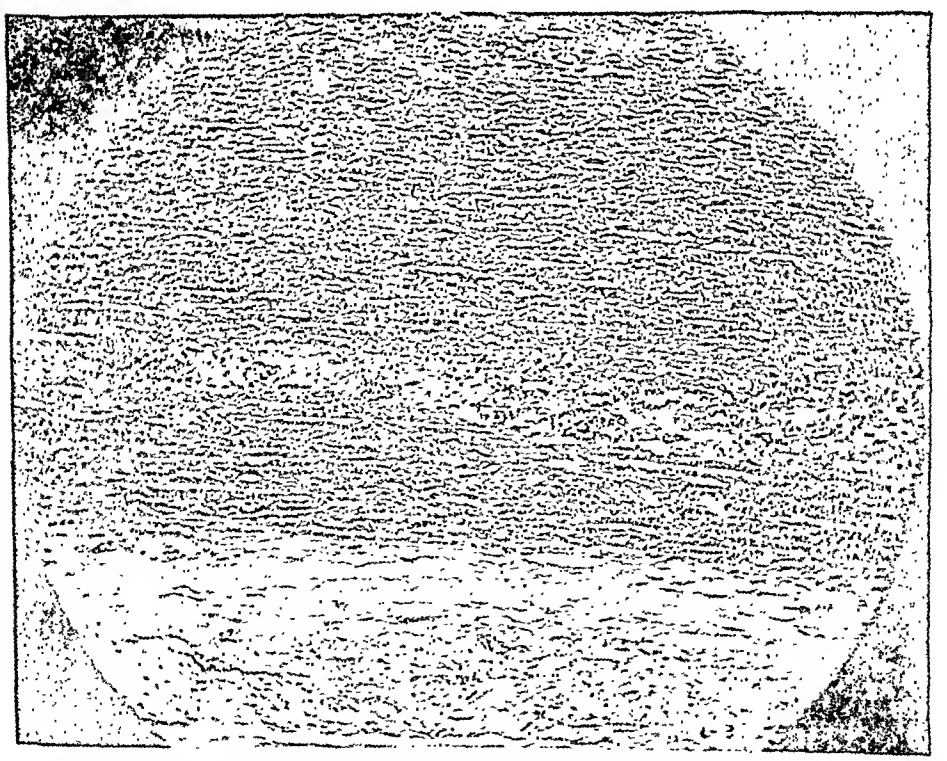


FIG. 6.—Section of thoracic aorta media (iron hæmatoxylin, van Gieson and Verhoef): atrophy of elastic fibres with hyalinization and increased vascularity at the junction of the outer with middle third of the media. Magnification : × 97.

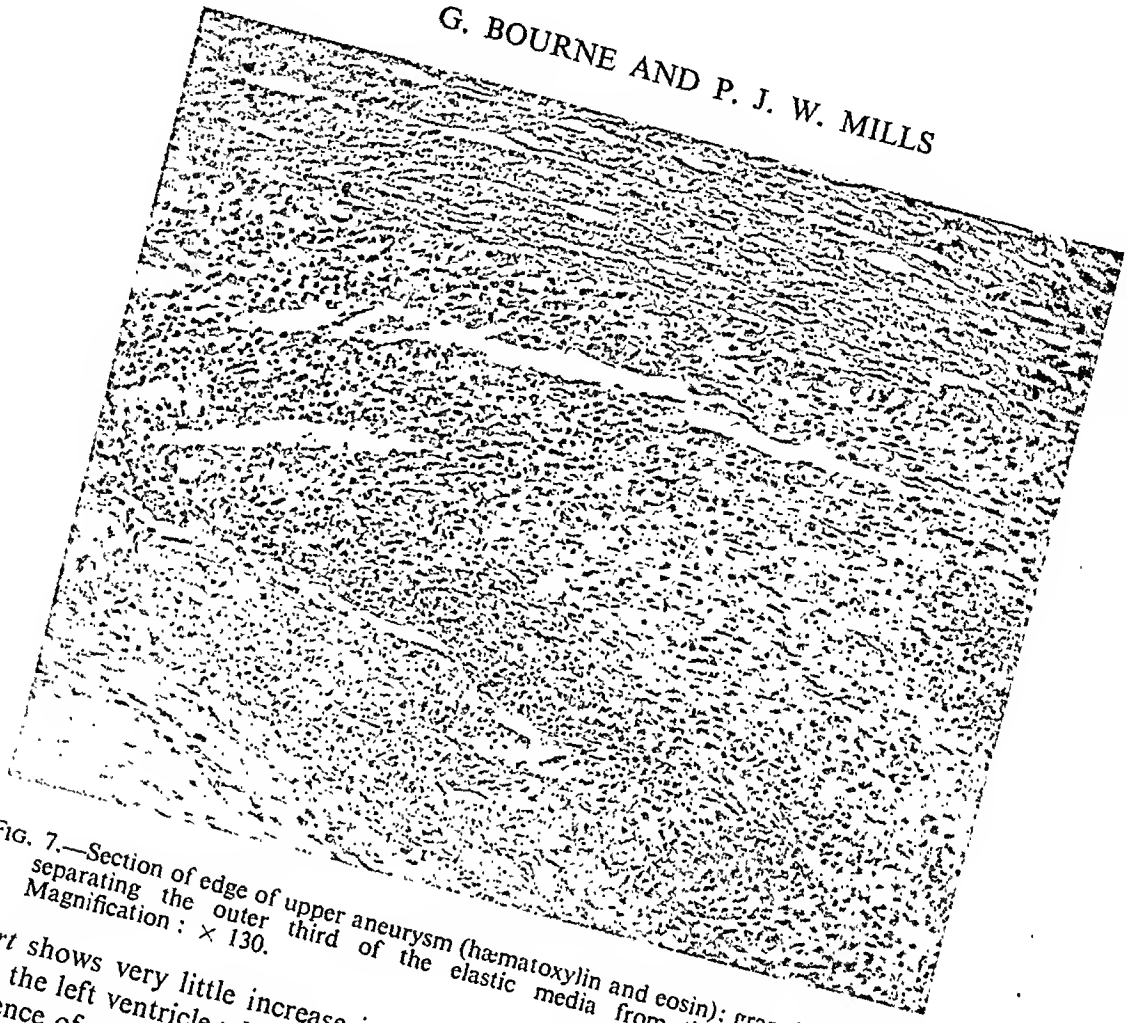


FIG. 7.—Section of edge of upper aneurysm (hæmatoxylin and eosin): granulation tissue separating the outer third of the elastic media from the inner two-thirds. Magnification : × 130.

The *heart* shows very little increase in interstitial fibrous tissue except for subepicardial pale areas in the left ventricle which consist of ancient acellular collagen.

The sequence of events appears to have been first a chronic degenerative hyalinization of the middle coat of the aorta, secondly acute hæmatoma formation in the media at the junction of middle and outer thirds, thirdly rupture of the underlying intima, and fourthly dissection of the vulnerable media by the inrushing aortic blood with the formation of dissecting aneurysms. In this case there is no doubt that atheroma has played an important role in the localization of the site of primary intimal rupture.

SECOND CASE REPORT

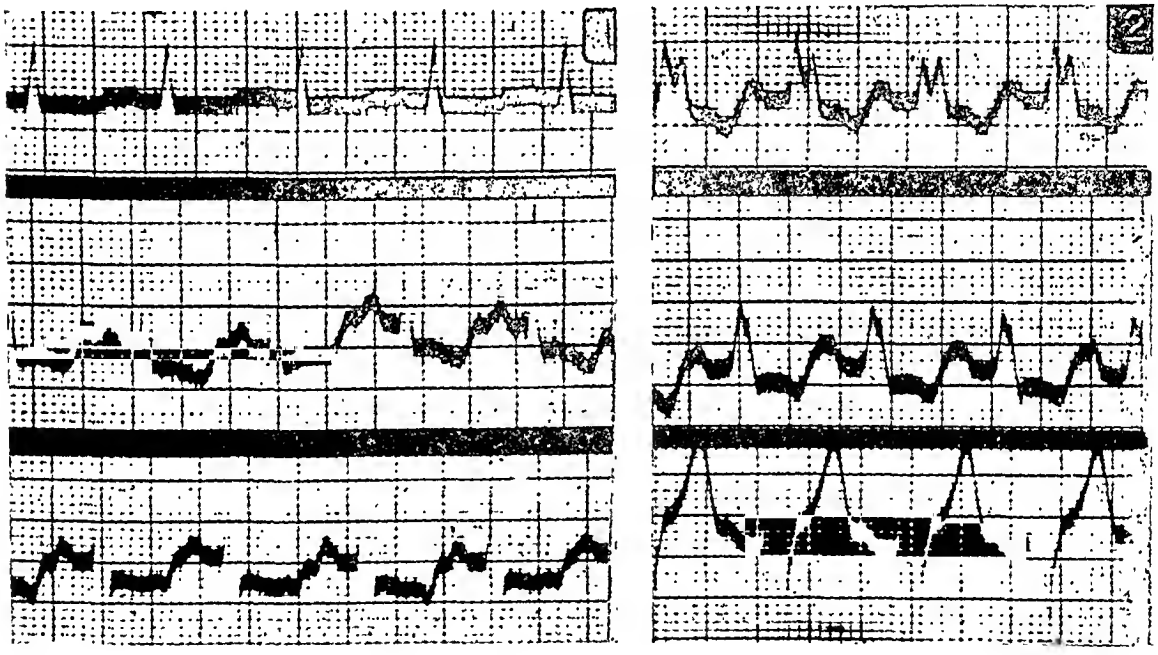
A housewife, aged 36, had for a period of ten weeks before admission been complaining of pain below both shoulder blades and upon each side of the neck. She suffered from this pain in attacks which would pass off, and they might be associated both with nausea and with giddiness. She was not short of breath in the intervals between the attacks, but noticed some dyspnœa at the time. The original attack occurred while she was ironing, and the pain and discomfort were severe enough to need the attention of a doctor. This attack lasted throughout the day and increased in severity until she vomited in the evening. Since the first attack she had felt what she described as a lump in her throat, which was present all the time and especially noticeable on swallowing.

Five weeks before admission, on getting up in the morning she had a particularly severe attack associated with intense nausea. She recovered, however, and continued up and about, feeling fairly well except for slight recurrent attacks of the nature described above. She had no cough, no pain in the front of the chest, no hæmoptysis nor interference with breathing. Her appetite had been good and there were no other complaints. On the morning of admission she was seized with a more severe attack than she had previously suffered, and was admitted lying flat on a stretcher, intensely cyanosed, with a raised respiration rate and grunting expiration. There was no stridor. She also complained of numbness in the left arm, and kept her eyes closed because of intense vertigo.

On examination, which was limited in thoroughness by the patient's very distressed condition, the following outstanding points were noticed at this time. There was no orthopnœa. Cyanosis was intense; arterial and venous pulsation in the neck vessels was more than normal. The apex beat was outside the mid-clavicular line and was firm and normal in character. There were no murmurs. There appeared to be some slight diminution in the volume of the respiratory murmur at the right apex, and râles were present over the right chest. In other respects the lungs and pleuræ seemed to be normal. Later in the day the patient became extremely short of breath with increased cyanosis and with stridor. She was very restless. She then spat up a quantity of thick, frothy, unstained sputum, and was given morphia 1/6th, and atropine 1/100th of a grain, and oxygen by B.L.B. mask. She improved during the next 48 hours. Two days after admission the increased pulsation was still visible in the neck, the heart sounds were still normal, but in addition a triple friction sound was audible all over the præcordium, and especially in the area between the apex beat and the left sternal border. The blood pressure was 94/40, the heart rate 112, and the respiration rate 40.

During the day the patient became comatose and died.

The electrocardiogram taken on the day of admission (Fig. 8A) showed flattening of T I and well-marked S–T deviation downwards in leads I, II, III, and IV. The tracing taken two days later (Fig. 8B) showed the development of a left bundle branch lesion. The X-ray



A B

FIG. 8.—(A) Taken on day of admission, showing S–T deviation downwards in leads I, II, and III. T flat in lead I. (B) Two days later, showing left bundle branch defect.

film (Fig. 9) showed deviation of the trachea to the right at the level of the sterno-clavicular joints. Behind the left joint was a shadow corresponding to the post-mortem demonstration of an extension of the dissecting aneurysm along the origin of the left subclavian artery. The right lung was less translucent than the left, and the radiologist suggested the possible presence of some scattered consolidation, possibly in relation to an infarct. The right pulmonary artery was very prominent. These radiological differences between the two sides of the chest corresponded to the difference in physical signs. Such change could easily be produced by central mediastinal changes causing interference with the pulmonary arterial or venous systems. The heart showed no radiological evidence of increase in size.

FIG. 9.—Heart within normal limits. Aortic shadow extended to left subclavicular region, corresponding to site of subclavine extension of aneurysm. Right pulmonary artery abnormally prominent. Increased vascularity of middle and lower zones of right lung.

Post-mortem Examination

The body was well nourished. Head and neck were normal.

Thorax. On drawing forward the mediastinal contents the aorta was seen as a thickened, shaggy-looking structure. The thickening was due to a dissecting aneurysm, which had completely stripped the outer from the inner coats at the level of the ascending portion of the aorta. The dissecting blood formed a larger mass of organizing clot, probably six weeks old; this mass extended proximally to within half an inch of the aortic valves and also along an inch of the left subclavian artery; a longitudinal slit, one-quarter of an inch in length with sharp edges as though cut with a knife, was seen in the intima; it was situated at the distal end of the solid organizing clot, i.e. at the junction of the ascending and transverse arches of the aorta. The dissecting mass of fluid blood extended to the aortic bifurcation. Distal to the slit in the intima wall the dissecting blood was dark and fluid; it could be pressed back through the slit. The aortic lumen was reduced to the size of a crow quill.

Heart. The heart was not enlarged. The coronary arteries were not involved in the aneurysm. Dr. Discombe stated that atheromatous plaques did not involve the mouths of the coronaries but were present along their lengths. There was no evidence of any coronary infarction. Terminal focal necrosis of a marked degree was present. It is possible that in the intact organ the tumour formed by the extravasated blood could have pressed on the coronary arteries although it did not directly involve them. This pressure would have interfered more with the left coronary and the anterior descending branch. Myocardium, normal macroscopically. A minimal quantity of clear pericardial fluid present. Surfaces normal. Valves normal. Aorta, no atheroma, intima healthy.

Lungs both oedematous. Liver congested; stomach congested slightly; otherwise no abnormality of the gut.

Microscopically the heart muscle showed focal necrosis. The affected fibres were swollen and had lost their transverse striation and were more deeply eosinophilic than normal. Nuclei had disappeared and there were small numbers of polymorphs infiltrating the necrotic areas and an increase in epimysium cells. Dr. Discombe stated that the focal necrosis in the heart was most remarkable.

Discussion

There would thus appear to be no clear correlation between the post-mortem findings and the electrocardiographic changes. In neither case was there any evidence of occlusion or gross narrowing or infarction of the coronary circulation. In Case 1, both aneurysms were situated in the descending aorta. It was impossible to determine from the post-mortem reports of either case whether the presence of the dissecting aneurysms could have displaced or twisted the heart in such a way as to interfere with the coronary flow, but the radiological evidence in Case 2 did not support this hypothesis. In each case the cardiogram was very suggestive of posterior coronary infarction: in Case 1 there were changes in the ten days interval between the first and second tracings that strongly favoured a coronary occlusion; in Case 2 the bundle branch tracing that developed may have been a manifestation of the dying heart, since it was present on the day the patient died, but the previous curve showing S–T depression was taken two days before the patient died.

Unfortunately few electrocardiograms have been studied in dissecting aneurysm of the aorta because the patient so frequently dies before one can be taken. In 19 cases studied by Glendy, Castleman, and White (1937), only 2 had cardiograms taken; one of these was normal and the other showed changes suggestive of posterior coronary infarction, but in this instance it was found post-mortem that the aneurysm involved the mouths of the coronary arteries. This was not so in our two cases.

If the changes were due to the great lowering of blood pressure only (Katz, 1941), they should have been present in the cardiogram taken twelve hours after the second severe attack, when the blood pressure was at its lowest: but they were not present. The fibrous patches in the left ventricle in Case 1 were seen on section to be acellular and, therefore, of considerable standing; but in Case 2 the myocardial necrosis may have been significant. If these three possible causes are ruled out, it is difficult to explain the cardiographic changes.

In Case 1, the first attack of pain radiating to the back probably occurred at the time of formation of the upper aneurysm; the second, with characteristic tearing pain, persistent pain in the back, and subsequent dysphagia can be well correlated with the anatomical findings of the lower aneurysm of the thoracic aorta. It was this clinical picture that supported the correct diagnosis after the second attack, especially in view of the persistent pain in the back, an unusual symptom in coronary thrombosis. This case is also atypical in the site and multiplicity of its aneurysms.

The pathological findings in Case 1 strongly suggest that the aneurysms were preceded by hæmatomas produced by rupture of vasa vasorum into a media deficient in elastic fibres. A greatly increased vascularity of the wall of atheromatous vessels with a tendency to intramural hæmorrhage has been well described by Winternitz, Thomas, and LeCompte (1938). The majority of dissecting aneurysms arise in the ascending aorta and, in the absence of local atheroma, upon a basis of cystic medial necrosis coupled with hypertension; it does thus appear that in the descending aorta atheroma, by its associated increased mural vascularity, may play an important if indirect part in the pathogenesis of medial hæmatomas. In addition, advanced atheroma leads to pressure atrophy of the media, and finally may also determine the site of primary intimal rupture.

Summary and Conclusions

The most striking feature, and one not previously described, is the misleading influence of the electrocardiogram in the diagnosis of these two cases of dissecting aneurysm. The changes in it, when associated with the rest of the clinical picture, were sufficiently typical of myocardial infarction to mislead attention from the correct diagnosis. Thus the assumption that such changes are absent in dissecting aneurysm may be false.

The most important points in the differential diagnosis would seem to be as follows. The pain in both cases was referred to the back to a considerable extent, this pain was periodic and extended over a period of as long as 15 weeks in Case 2, with periods of remission. Absence of shortness of breath in an ambulatory patient would also be an important point. Evidence of mediastinal mechanical change should also arouse suspicion of a dissecting aneurysm. The numbness in the left arm and the lump in the throat in Case 2, and the dysphagia in Case 1, all bring out this point. The severity of the pain is such that few conditions other than coronary infarction are likely to be suggested. A pain of similar severity may occur in acute pancreatitis, but here it is the lower part of the back rather than the interscapular area that is the site of the pain.

The post-mortem investigations and notes in Case 1 were the work of Dr. I. Doniach of the British Postgraduate Medical School, Hammersmith; those of Case 2 were the work of Dr. George Discombe of St. Bartholomew's Hospital.

We are grateful to them for permission to publish these; and express our thanks to them for their help, and also to Dr. McMichael of the British Postgraduate Medical School for his kind co-operation in Case 1.

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CHRONIC DISSECTING ANEURYSMS

BY

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Received May 20, 1946

939 East was able to find records of only 27 instances in which the diagnosis of dissecting m had been made during life. Usually death from complete rupture of the aorta follows the initial dissection; of the 300 cases collected by Shennan (1934) 210 died week and survival for more than a year was recorded in only 16 cases. We have, e, thought it desirable to record two cases in which the diagnosis was made during e patient survived for three years and the other is alive and comparatively well eight ter radiographic recognition of the aortic lesion.

Case Records

1. In December 1943, a married woman, aged 55, was admitted to the Manchester nfirmary under the care of Dr. Crighton Bramwell, on account of severe pain in the the chest and in the lumbar area. Apart from an attack of smallpox when 4 and an n for uterine prolapse when 41, she enjoyed good health until the age of 52 years. then suddenly seized by severe stabbing pain in the left anterior chest which radiated eft scapular region and the dorso-lumbar area. She fell to the ground but did not sciousness. She was confined to bed for two weeks and suffered from some aching the left chest for four or five weeks. Subsequently she remained well for nearly when a similar attack took place; her blood pressure was then found to be 230/130. ng this attack her pain again gradually disappeared and she remained in comparatively alth for a year, when her third attack of severe pain occurred. She was admitted to and the heart and aorta were found to be enlarged radiographically. On this occasion, , her pain did not subsequently disappear, but extended to the lumbar area. After months of persistent pain in the chest and back she was admitted to the Manchester nfirmary in April 1943, under the care of Dr. Oliver. Her blood pressure was then in the right arm and 195/130 in the left. Cardioscopy showed gross dilatation of the The Wassermann reaction was negative and a diagnosis of chronic dissecting aneurysm de. She remained in bed for four months, but was never free from pain. When she walking 20 yards brought on severe anginal pain; this gradually improved, but in ber 1943 she began to suffer from attacks of palpitation of sudden onset, lasting hours. She was readmitted under the care of Dr. Bramwell. Her blood pressure was 5/140 in the left arm and 210/140 in the right. On cardioscopy the aorta was grossly and the left ventricle enlarged (Fig. 1 and 2). The blood Wassermann and Kahn s were negative. A cardiogram showed left axis deviation and biphasic T waves in leads I and II, with depression of the corresponding RS–T segments; these nces were attributed to left ventricular strain associated with her hypertension. n hospital she had several attacks of palpitation, during one of which a cardiogram paroxysmal auricular tachycardia at a rate of about 160 a minute. These attacks e stopped at once by carotid sinus pressure, but the ectopic rhythm was re-established inutes after pressure was released. While in bed her pain diminished but did not ier disappear. Some eight weeks after admission, and shortly before she was to go he collapsed in the lavatory and fell to the ground semi-conscious, with an imperceptible She improved slowly but complained of severe pain in the left chest; four days later denly collapsed and died within a few minutes.

cropsy was performed nine hours after death. Apart from slight passive congestion of ominal viscera, the abnormalities were confined to the thorax. The left pleural cavity ed with straw-coloured fluid and blood clot; this had led to collapse of the left lung.

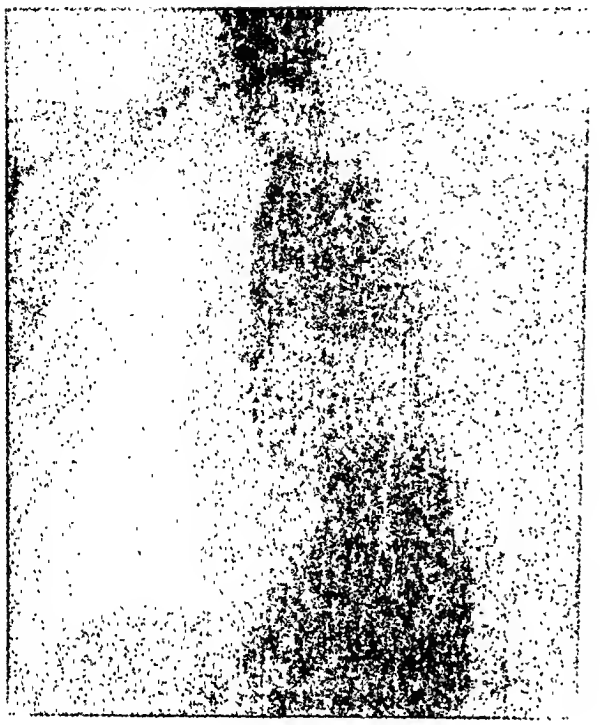

FIG. 1.—*Case* 1. Postero-anterior teleradiogram. The heart outline can be seen in front of the shadow of the greatly enlarged aorta.

FIG. 2.—*Case* 1. Left anterior (II) oblique radiogram, showing the great size of the descending thoracic aorta. The aortic window is still visible for the ascending aorta is not greatly enlarged.

The heart weighed 390 g., the left ventricle was hypertrophied but not dilated, and there were many pearly-grey areas of myocardial fibrosis. The right ventricle and all the valves were normal. The circumference of the aortic orifice was not increased (6 cm.). Numerous atheromatous plaques were present in both coronary arteries but the lumen was not severely narrowed at any point.

Externally the aorta was greatly dilated from just below the origin of the left subclavian artery to the level of the diaphragm (Fig. 3). At about the middle of the lateral surface of the dilated portion there was a transverse tear, 2 cm. long, where the aneurysm had ruptured into the left pleura. On opening the aneurysm (Fig. 4) two channels were seen; on the inner border a narrow, flattened channel (A) led from the normal arch of the aorta to a dilated blind sac, in which the orifices of the last two pairs of aortic intercostals could be seen; this narrow channel was, therefore, the compressed descending thoracic aorta. The second channel (B) formed the greater part of the specimen and was continuous with the arch of the aorta above and with the abdominal aorta below. It was partially lined by laminated thrombus (C) and the external tear communicated with it. Where the two channels arose from the arch of the aorta the free edge of the septum separating them was rounded and smooth and continuous with a ridge around the mouth of the larger channel (Fig. 4, inset); the free margin had clearly been separated from this ridge when the dissection started and, since both ridge and free edge were smooth and healed, this separation was not recent.

Sections from the arch of the aorta, the walls of the aneurysm, and the abdominal aorta were stained with hæmalum and eosin, van Gieson, mucicarmine, Sudan IV, and Weigert's elastic stain. Sections from the aneurysm showed that at a and a′ (Fig. 5, see p. 195) the media had split, two-thirds of its tissue passing inwards to cover the septum between the two channels and one-third lining the outer wall of the larger channel; the aneurysm had thus arisen by a separation of the outer third from the inner two-thirds of the media. Within the intima of the original aorta (A), at its acute angles (near a and a′), there were polyhedral cells loaded with fat and between them large blood capillaries, while superficially a zone of young connective tissue and organizing blood clot invaded the original lumen of the aorta; in time this process could have obliterated the lumen of the compressed aorta. The lateral wall of the aneurysm was lined by dense fibrous tissue covered in some places by endothelium, in others by organizing thrombus.

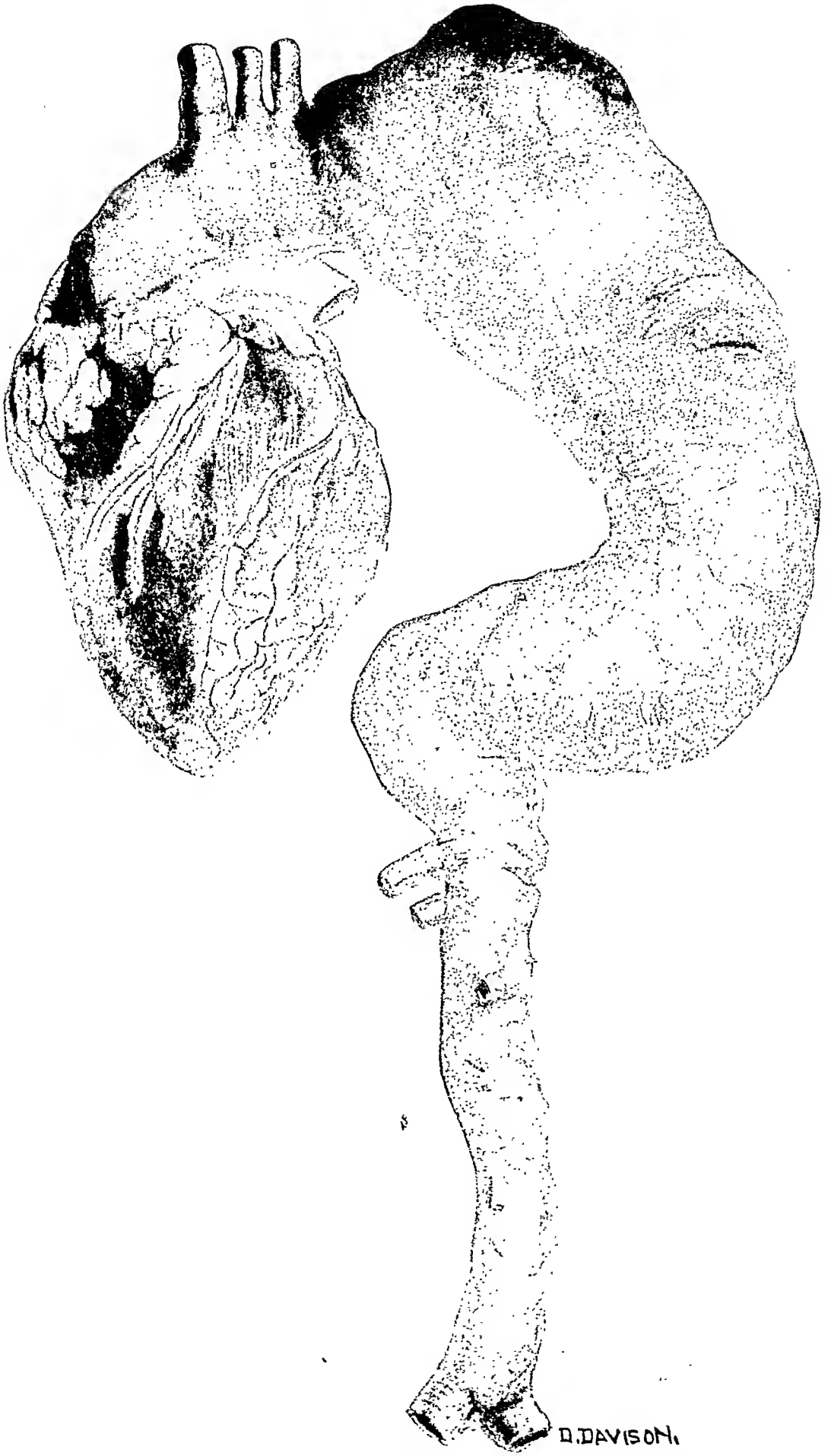

FIG. 3.—*Case* 1. The aneurysm from a water-colour painting. The transverse tear is visible on the left border of the aneurysm. The aneurysm does not extend below the diaphragm. The ascending aorta and the abdominal aorta are not enlarged.

FIG. 4.—*Case* 1. The opened aneurysm, from a drawing. *A* is the compressed lumen of the descending thoracic aorta which ends in a blind sac at the level of the diaphragm. This sac has been opened and in it can be seen the orifices of two of the four intercostal arteries which communicated with it. *B* is the aneurysmal sac, which communicates with the arch of the aorta above and the abdominal aorta below. *C* is a laminated thrombus lining part of the wall of the aneurysm.

An unusual feature was the presence of atheromatous plaques on the wall of the aneurysm; these have been previously described in a dissecting aneurysm by Weiss, Kinney, and Maher (1940).

In the arch of the aorta there were striking medial degenerative changes for many small cyst-like spaces were seen and an excess of mucin was present, particularly around the cysts. Similar, though less striking, changes were also found in the media of the wall of the aneurysm, but they were not present in the abdominal aorta. The medial degeneration was thus most striking proximally, unlike the atheromatous changes which were very slight in the arch but of moderate severity in the abdominal aorta. There was no evidence of destruction of elastic tissue apart from a few complete breaks at the angles of the compressed aorta. The adventitia and vasa vasorum were normal and there was no suggestion of syphilis of the aorta.

The aneurysm appeared to have developed from the entry of blood into the media just beyond the origin of the left subclavian artery; the media was split at the junction of its outer third and inner two-thirds and the dissection extended until the diaphragm obstructed its advance. The pressure in the aneurysmal sac led to compression of the original aortic lumen and to the re-entry of the aneurysm into the aorta below the compressed portion. Thus the blood supply to the legs and abdomen, transiently interrupted by occlusion of the aorta, was restored by re-entry of the aneurysm and the aneurysmal sac took up the original function of the aorta. Healing of the aneurysm followed; first by organization of the clotted blood lining

its walls, then by the development of a lining of endothelium. Finally, reparative processes began in the angles of the compressed aorta; this process, if continued, would have led to obliteration of the functionless lumen.

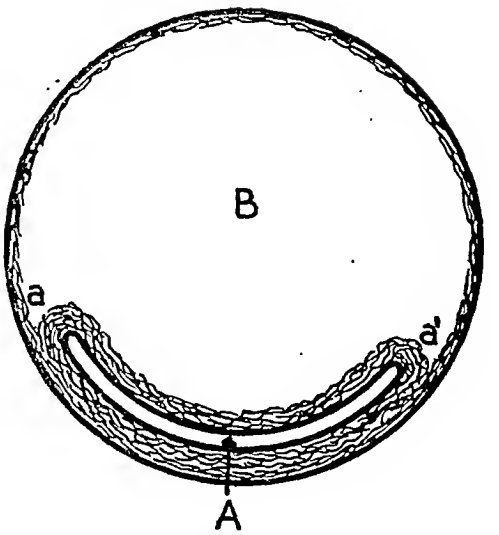

FIG. 5.—*Case* 1. Diagrammatic transverse section of the aneurysm. At a and a' the media has split, one-third of its tissue lining the outer wall of the aneurysmal sac (B), and two-thirds covering the septum between the aneurysmal sac and the compressed lumen of the aorta (A). The aneurysm was, therefore, formed by splitting the media.

Case 2. In 1939, a single woman, aged 36 years, was admitted to the Manchester Royal Infirmary under the care of Dr. Crighton Bramwell, complaining of palpitation and breathlessness. Apart from measles as a child, she had been well until 1933, when she was a probationer nurse, aged 30 years. She then began to suffer from severe pain in the back which was treated by radiant heat and massage and disappeared after several months. In January 1938 she developed acute bronchitis; during this illness she awoke one night with a severe attack of palpitation and subsequently suffered from dyspnœa, palpitation, and lassitude. Some weeks later chest radiograms were taken and an enlarged substernal thyroid was diagnosed; she was treated with Lugol's iodine without benefit. In April 1938, while on sick leave in Ireland, she was admitted to hospital on account of her dyspnœa and palpitation. Her blood pressure was found to be 200/140 and radiograms of the chest showed moderate cardiac enlargement and considerable dilatation of the aorta. She was treated by X-ray therapy to the sternal area, but this was followed by intense pain in the back. While in hospital she had a uterine hæmorrhage and underwent a myomectomy for uterine fibroids; after operation she had periods of mental confusion and amnesia, and severe paroxysms of palpitation. In September, while trying to make her bed, she suddenly collapsed, and in December 1938, developed sudden severe dyspnœa with evidence of circulatory collapse. In March 1939 she returned to Manchester and remained in bed until she was admitted to hospital in May owing to a severe attack of constricting chest pain which was followed by vomiting. Subsequently she had three similar attacks and in September developed acute bronchitis with hæmoptysis. A fifth attack of constricting chest pain followed this illness and in October 1939 she was admitted to the Manchester Royal Infirmary.

On examination the pulse rate was 120 and her brachial blood pressure 200/140; the same reading was obtained in the legs and there was good pulsation of the dorsalis pedis arteries. The heart sounds were very loud but no murmurs were present. Cardioscopy showed some enlargement of the left ventricle and considerable diffuse enlargement of the thoracic aorta (Fig. 6) with calcified plaques in its wall (Fig. 7). Kymography revealed quite good pulsation of the descending aorta. A cardiogram showed striking left axis deviation associated with biphasic T waves (− +) in leads I and II and depression of the corresponding RS–T segments; these appearances were attributed to left ventricular strain associated with her hypertension. The blood Wassermann and Kahn reactions were negative and the urea clearance 75 per cent of the average normal. The condition was thought to be a chronic dissecting aneurysm.

While in hospital she suffered from severe aching pain in the left scapular region, headache, and palpitation. On several occasions she became confused and disorientated. Her condition had slightly improved when she left hospital in January 1940, but she continued to suffer from pain in the back and headaches until she was readmitted in December 1940, owing to the increasing severity of her pain and the onset of aching pain in the left leg. After her return home she remained in fair health, apart from the pain, until April 1941 when her right arm and leg became paralysed while she was out walking. The paralysis rapidly improved but some weakness of the right arm remained. In May she had a severe attack of sharp pain in the back of the chest, just to the left of the spine and in the left infra-scapular area. Subsequently she suffered from constant aching pain in this area with recurrent severe attacks of sharp pain, often precipitated by exertion. In August, severe aching pain developed in the epigastrium, and in November 1941 she was readmitted to hospital owing to the severity of her epigastric and chest pain. Her brachial blood pressure was then 165/110 and the dorsalis pedis pressure 205/110. While in hospital she had two sudden severe attacks of

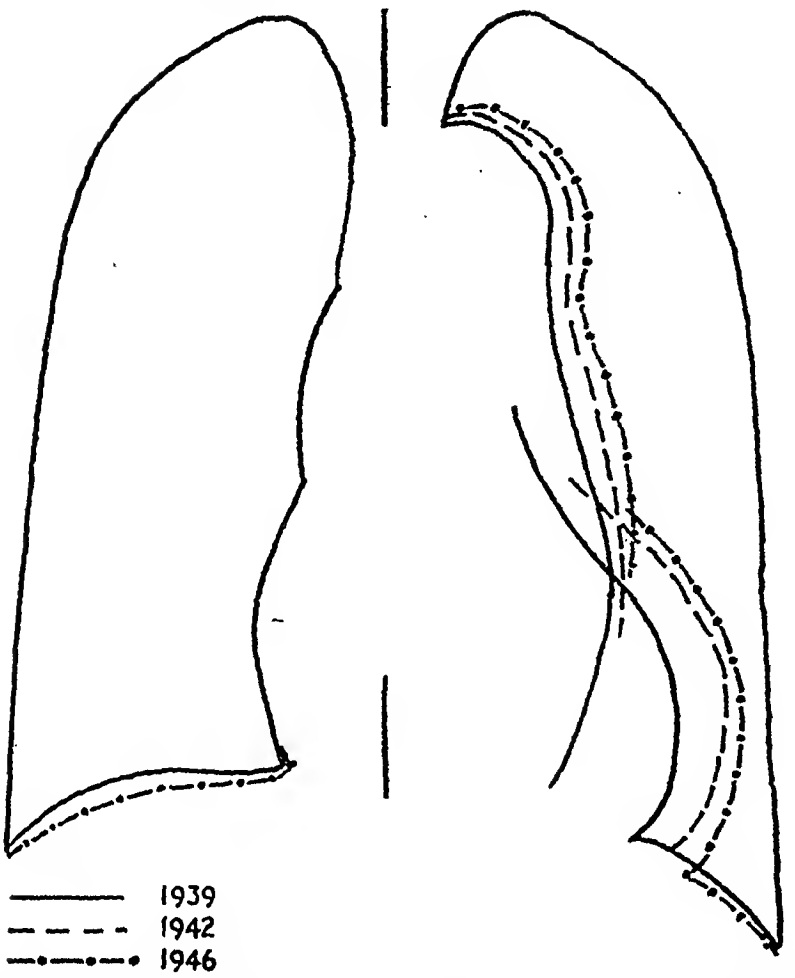

FIG. 6.—*Case* 2. Outline drawings from postero-anterior teleradiograms, 1939, 1942, and 1946. The chest outlines were almost identical in all three radiograms and there has been little change in the contour on the right side of the cardiac silhouette. The gradual enlargement of the left ventricle and of the aorta is shown.

"grinding" pain in the left chest, relieved only by morphia, and followed by nausea and vomiting.

After her return home the pain continued to increase in severity and by March 1942 had become intolerable. When she was readmitted to hospital she complained of constant aching pain in the lower costal and lumbar region with several severe exacerbations each day, relieved only by morphia, and sudden attacks of constricting sternal pain, terrifying in character, but unrelated to exertion. The severity of these pains and the gradual deterioration in her condition demanded radical measures and paravertebral proctocaine injection of the upper 8 dorsal interspaces on both sides was attempted after a successful novocaine test. Unfortunately, the proctocaine injection failed to give much relief, and in August, Mr. Geoffrey Jefferson undertook paravertebral alcohol injection. After operation her pain remained severe for some weeks and she developed hyperæsthesia of the lower left thoracic root areas, fæcal and urinary incontinence, and pyramidal signs. Nevertheless, her pain gradually diminished and a year later, in August 1943, she was almost entirely free from pain and her neurological signs and symptoms had completely disappeared.

In 1944 she suffered from depression and was reluctant to get out of bed, but during the whole of 1945 she was active, undertook a great deal of housework and cooking and went to dances; she was entirely free from pain, gained weight, and lost all interest in her illness. In December 1945, however, cardioscopy showed some increase in the size of the heart and aorta and in the calcification of the aortic wall (Fig. 6, 7, and 8). Lateral and oblique radiograms of the thoracic spine did not show any erosion, the blood Wassermann reaction was negative, and the urea clearance 74 per cent of the average normal. It was noted that the right radial pulse was poorer than the left; the blood pressure in the right brachial artery was 200/125, in the left 215/125, and in the left dorsalis pedis artery 240/125.

FIG. 7.—*Case* 2. Postero-anterior teleradiogram, December 1945. Calcification can be seen in the enlarged aortic knuckle.

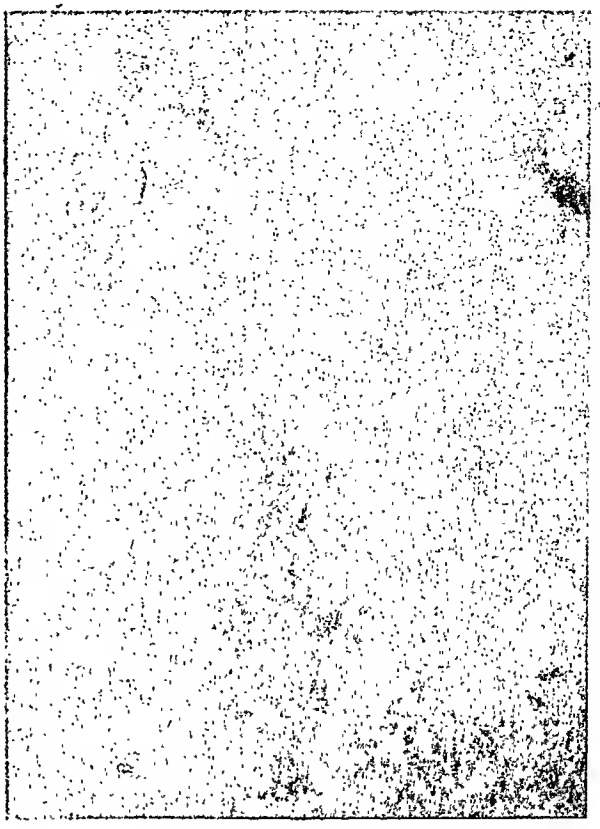

FIG. 8.—*Case* 2. Right anterior (I) oblique radiogram showing calcification of the enlarged aorta.

In January 1946 she was readmitted with acute bronchitis, from which she made an uneventful recovery.

DISCUSSION

Virchow and other pathologists of his time thought that dissecting aneurysms arose from the dissection of blood through the floor or edge of an atheromatous ulcer. Subsequently this opinion was criticized by many pathologists and Shennan (1934) has reviewed the subject fully. In his own series Shennan found that only 6 of 218 recent dissecting aneurysms appeared to have started from an atheromatous ulcer: he emphasized the importance of medial degenerative changes, particularly those involving the elastic laminæ, and believed that the media nearly always gave way before the intima. Rottino (1939) studied the distribution of medial degenerative changes in 12 dissecting aneurysms and found that these changes were confined to the ascending and transverse aorta in 11 cases; this is probably significant for it is in these sites that the majority of dissecting aneurysms begin. Sailer (1942) studied and classified the types of medial degeneration that occur in the aorta. The histological appearances in our Case 1 are in general agreement with the views expressed by Shennan (1934) and Rottino (1939), and the degeneration is similar to that in certain of the types described by Sailer (1942).

Since survival for more than a few days is the exception when the aortic media is shattered by a sudden hæmorrhage, it is interesting to consider the factors that may avert death. Shennan (1934) found that death was due to external rupture in 195 (95 per cent) of 206 dissecting aneurysms that did not survive for more than a few days. If death is to be postponed it seems clear that some event must take place to make external rupture unlikely, and this can only be the relief of pressure in the aneurysmal sac. This happens when, as in Case 1, the aneurysm ruptures internally, so that the blood flow re-enters the original lumen of

the aorta. The effect of re-entry on the period of survival is shown in Table I, which is compiled from Shennan's (1934) figures.

TABLE I

EFFECT OF RE-ENTRY ON THE PERIOD OF SURVIVAL

	Number of cases	Survival for less than 5 weeks	Survival for more than 5 weeks
No re-entry	199	192 (96%)	7 (4%)
Re-entry	92	26 (28%)	66 (72%)

Re-entry is, therefore, almost a pre-requisite of survival, for if it does not take place 96 per cent of patients die within five weeks, whereas when the circulation is re-established in this way only 28 per cent die in the first five weeks. Table I also shows that if the patient survives for more than five weeks, re-entry has taken place in 90 per cent (66 of 73 cases). This observation has an important bearing on the diagnosis of chronic dissecting aneurysm. In acute dissections East (1939) has emphasized the almost pathognomonic changes in the circulation of the legs due to obstruction of the aorta, which often afford convincing clinical evidence of the diagnosis. But when re-entry takes place the circulation is re-established in the legs; there will, therefore, be no evidence of aortic obstruction in 90 per cent of cases after the fifth week. Our Case 2 is an example of this, for the blood pressure in the legs was at least as high as that in the arms.

Shennan (1934) pointed out that re-entry into the original lumen is particularly liable to occur when the dissection reaches some obstruction, since this will increase the pressure in the aneurysmal sac. Mayr (1925) claimed that re-entrance usually took place into the iliac arteries, where the division of the aorta obstructs the progress of the dissection. The point of re-entrance was noted in 61 cases in Shennan's series; 43 aneurysms re-entered the pelvic branches of the aorta. Our Case 1 is an example of an unusual site of re-entry, for the extension of the aneurysm was prevented by the diaphragm and re-entry occurred at that level.

It was suggested by Bostrom (1888) that re-entry always prevented external rupture. This claim is not confirmed by our Case 1, and was criticized by Shennan for of 92 cases in his series in which re-entry occurred, external rupture also took place in 39 (42 per cent). On the other hand, when re-entry did not occur, external rupture took place in 95 per cent. Thus, although re-entry is no guarantee against external rupture, it does afford a considerable measure of protection against that fatal complication. Indeed, if re-entry takes place and the patient survives for more than a few weeks, there is a good chance that the aneurysm will not subsequently rupture. This is shown in Table II by an analysis of the causes of death in chronic dissecting aneurysms based on Shennan's (1934) figures.

TABLE II

CAUSES OF DEATH IN 79 CHRONIC DISSECTING ANEURYSMS

Heart failure	34
Hæmorrhage from aneurysm	16
Chronic nephritis	8
Cerebral hæmorrhage	6
Miscellaneous	11
Obscure or unknown	4
Total	79

In our Case 2 there is, therefore, no reason to believe that the aneurysm must ultimately rupture, and survival has been recorded for more than 30 years (Graham, 1886).

SUMMARY

Two cases of dissecting aneurysm, diagnosed during life and surviving in one case for three years and in the other for at least eight years, are described. The importance of re-entry in averting fatal rupture of the aneurysm is discussed, and its significance in the diagnosis of chronic dissecting aneurysm is indicated.

We are indebted to Professor Crighton Bramwell and to Professor S. L. Baker for their interest and advice and to Dr. E. Duff Gray for the radiograms. Professor Bramwell has kindly given permission to publish details of these cases, which were under his care.

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DISSECTING ANEURYSM WITH SURVIVAL FOR THREE MONTHS AFTER RUPTURE INTO THE PLEURA

BY

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From Guy's Hospital

Received June 12, 1946

The following case of dissecting aneurysm is recorded because the patient survived for three months after a considerable amount of blood had ruptured into the pleural cavity.

It is hard to write of any aspect of dissecting aneurysm without making use of Shennan's (1934) monumental review of 300 cases. In recent dissecting aneurysms external rupture is much the most common cause of death. Where the intrapericardial aorta was involved (177 cases) rupture took place into the pericardium in 152, into the pleura in 6, and into the mediastinum in 5 cases. Where the aneurysm was completely extrapericardial (41 cases) rupture into the pleural cavity was relatively more common—into the left pleura 13 cases, into the mediastinum and pleura (generally left) 11, into the mediastinum 2, and into the lung 1 case. In the old "healed" dissecting aneurysms (79 cases) heart failure was the commonest cause of death (34 cases) but rupture into one of the cavities occurred 16 times and in some of these it was into the pleura.

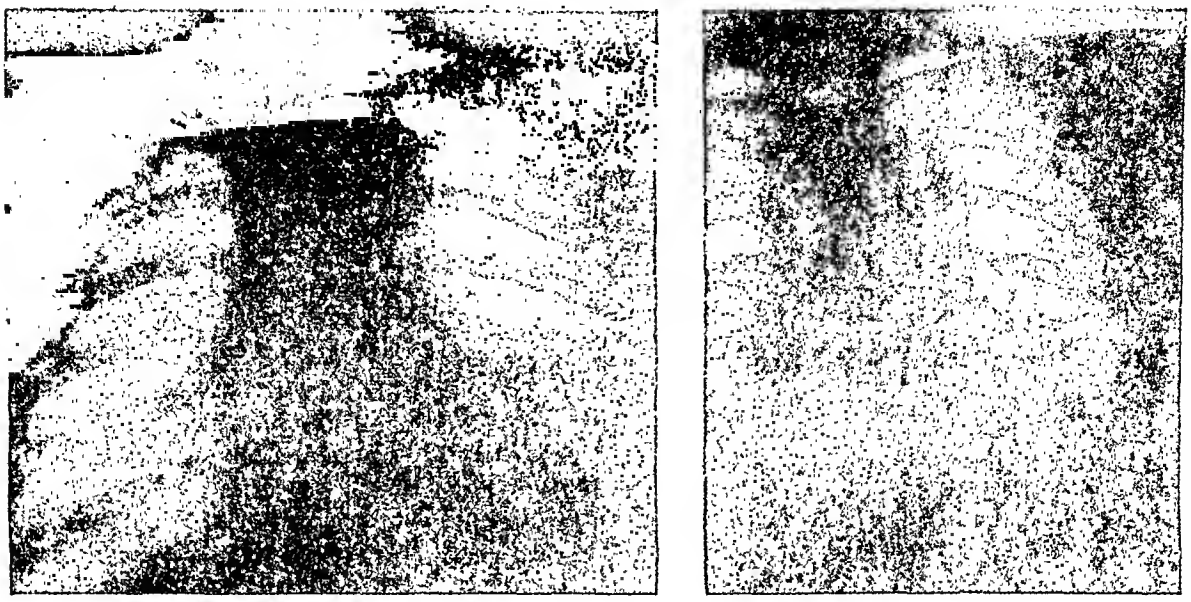
The following cases are the only references I have found in Shennan's monograph to hæmorrhage into the pleural cavities before the terminal episode, but his paper did not include a large number diagnosed during life. The case of Davy and Gates (1922) lived for 19 days and one of the reasons for the diagnosis was leakage of blood into the left pleura. The case of Barton (1930) lived for 17 days and fluid began to collect in the left pleura during the first day.

A woman was admitted to Guy's Hospital having collapsed after very severe pain in the chest and back with signs of fluid in the left chest. For ten years she had had occasional faints and for five years some pain on the left side of the chest, not clearly related to exercise. In September 1944 she had a right-sided hemiplegia from which she made a good recovery in a month; in December she had a similar attack, this time on the left side, and again recovered in the course of two months except for some slight residual signs.

On April 10, 1945, when 66, she was sitting on London Bridge Station waiting for a train when she was seized with agonizing pain in the centre of the chest and back. This was followed by breathlessness and collapse and she did not remember much about her admission to hospital. The blood pressure had fallen to 120/100 but soon rose to 220/130 and remained about this level after the first two days. The severest pain quickly subsided after morphia ($^1/_4$ grain and the same amount repeated) but she continued to have pain, especially in the back and needed a small dose of dilaudid ($^1/_{16}$ grain) most nights for some weeks. Her hæmoglobin had fallen to 55 per cent and there was a leucocytosis of 15,000 with a normal differential count.

Cardiac infarction was suspected but the cardiogram only showed slight inversion of T I and there was no significant change in this a week later. She was found to have a left-sided pleural effusion (Fig. 1A) and a week later aspiration showed almost pure blood, not merely a blood-stained effusion.

At this stage I was asked to see her and on these findings (with a loss of 3 stone during the previous three years) thought she must have a growth of the lung, possibly with a secondary deposit causing cardiac infarction, although the past cerebral history favoured primary cardiovascular disease and without the pleural effusion would have been taken as supporting cardiac infarction in spite of the absence of cardiographic support.



A B

FIG. 1.—Teleradiograms of the chest showing the wide aorta and large heart hidden in a left-sided hæmothorax. (A) 20/4/45, ten days after admission. (B) 14/7/45, three months after admission.

Progress. She made slow but steady progress although there was no significant change in the physical signs in the left lung. Five radiograms of the chest showed no great difference. The " aortic " shadow was wide but this was accepted as part of her atherosclerosis. After her death re-examination showed that the width had increased slightly from 8·5 to 9·5 cm.

After two months in bed she was allowed up and after another month was looking forward to going home. On July 10 she went to the lavatory and while there called and said she felt faint: her pain was not very severe but she collapsed and was carried back to bed. She became unconscious within a few minutes and died in half an hour.

Post-mortem examination. This was carried out by Dr. Hopkins to whom I am indebted for the specimen illustrated but the weights and full details of the other viscera were lost.

The brain was not examined. The kidneys were rather small and granular. The heart showed moderate hypertrophy of the left ventricle. The aortic valves showed some atheroma and calcification. The ascending aorta and arch showed slight atheroma only.

In the arch of the aorta, about midway between the origin of the subclavian artery and the level of the pulmonary artery there was a recent tear of the aorta about 3·5 cm. long, with an escape of blood into the lung and pleural cavity. This recent tear and the large amount of recent clot made it difficult to be sure if there had been an original tear here with rupture through to the lung and pleural cavity and downward dissection, or if the original leakage into the lung at this point had come from the lower tear (see later) with retrograde dissection back to this level.

Below this tear for at least 15 cm. there was an extensive dissection with stratified layers of blood clot, partially organized and looking of some months duration (i.e. probably from the time of the collapse and hæmothorax three months before). For 4 cm. below the tear (A to B, Fig. 2) there was a wider recent blood clot with a narrow tongue projecting a further 2 cm. (B to C), both on the inner side of the laminated clot, showing that the dissection had increased just before her death.

9 cm. below the fatal tear there was an old transverse tear 1·5 cm. long. The dissection extended below this and the stratified clot at this point looked at least as old as, and probably older than, anywhere else. This was certainly an old tear but it was not certain if it was the point of re-entry (though not the lowest point of the dissection) or, as seemed more likely, if it was the original tear causing the dissection that had spread upwards (as well as downwards) and had ruptured into the lungs and pleura near the point where the final tear had caused death. If this was so, it might explain why the second rupture into the pleural cavity had

FIG. 2.—Photograph of the upper portion of the descending aorta between the two tears. The original channel of the aorta has remained patent and the dissection is completely occluded with blood clot. On the inner side there is recent blood clot (from A to B) with a narrow tongue projecting down to C. On the outer side the blood clot is laminated and organized and near the lower tear the laminæ can be seen lying more horizontally and above this nore vertically. Above the upper tear part of the arch of the aorta has been cut away to show the blood clot penetrating into the lung.

caused death so quickly while the first had not. This uncertainty makes the case of little value except as an example of unusually long survival after a large hæmothorax had developed from a dissecting aneurysm.

SUMMARY

A case of dissecting aneurysm is described where the patient lived for three months with a large hæmothorax from the original tear and dissection of the aorta. She died suddenly from a second tear (also with some dissection) with rupture into the pleural cavity.

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DISSECTING ANEURYSM OF THE AORTA: A NEW SIGN

BY

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Received September 2, 1946

Ever since Shennan's (1934) masterly and comprehensive analysis of 317 cases of dissecting aneurysm of the aorta, including 17 of his own, interest in this condition has been steadily increasing, with the encouraging result of a mounting proportion of ante-mortem diagnosis. Shennan reported only 6 such correct diagnoses out of the 317 cases, up to and including 1932, and credited Swaine (1855–6) with being the first to make it. Reich (1944) reported a further total of 153 American cases since Shennan, 36 of which were diagnosed: he added 19 cases of his own but omitted Logue's (1943) remarkable series of 12 cases, of which 10 were correctly diagnosed. Thomas (1945) reported another case, also diagnosed during life. This alone brings the total up to 49 correct diagnoses out of 512 collected cases. The incidence of this disease as given by Shennan is one in every 175 autopsies. Reich in 1944 worked out the average incidence given by various writers as one in every 380 autopsies.

The effect of the stimulus Shennan provided has been kept alive by subsequent writings. This has resulted in a general change of attitude, to use the words of Glendy *et al.* (1937), "from one of remote academic interest in the pathological aspects of the subject to one of lively practical attention to the possibility of making an ante-mortem diagnosis." Apart from the description of new signs, the features that should provide a lead to the diagnosis have been amplified. The following case is recorded on account of its many interesting features. Diagnosis during life was expressed in these words: "Theoretically, the only diagnosis that would fit all the symptoms and signs of the patient is dissecting aneurysm of the aorta." In view of a suspicious peptic ulcer history during the previous year, however, and the presence of abdominal signs with release tenderness etc., an abdominal emergency, superimposed on a background of cardiovascular disease, could not be ruled out. Further, a sign, not hitherto mentioned in published writings, which promises to be of pathognomonic significance when present, will be described.

Case Report

A man of 71 years of age was sent into hospital with a short note from his doctor stating that the patient had a sudden attack of severe pain in his stomach the same day, and was thought to have a perforation of the stomach: $^1/_4$ of a grain of morphine sulphate had been given.

Seen by the resident surgical officer, the diagnosis of perforated peptic ulcer did not seem conclusive. Interrogation revealed that the patient was reclining in an armchair that morning, when suddenly he felt an extremely sharp and severe pain, a little below the umbilicus, soon spreading to the epigastrium and lower part of the chest, round both sides to the back, but not elsewhere. There was no retrosternal pain, and no nausea or vomiting. Slight dyspnœa was complained of. There was no disturbance of bowel movements, which had been regular up to and including that morning. For the past year he had some pain suggestive of peptic ulcer, which sometimes woke him up in the night and was often relieved by taking food. He also gave a history of high blood pressure for some time, and typical anginal pain, which he had experienced on four or five occasions; the pains came on with exertion and disappeared fairly quickly with rest.

On examination he showed an anxious pale face, and was obviously in severe pain, but could move about in bed. His temperature was subnormal and his respiration about 20 a minute. The abdomen was found to move well with respiration, but there was tenderness and guarding all over. Release tenderness was elicited as well, especially from the epigastric and right hypochondriac regions. There was no shifting dullness, no palpable abdominal mass, and no abnormal sounds on auscultation.

The heart was not obviously enlarged. A radiogram of the chest, however, taken the next day about two hours before death, showed a rather enlarged heart shadow with a widened supracardiac shadow. The heart sounds were faint but regular. There was persistent bradycardia of 44 beats a minute, but the previous rate was unknown. No murmurs or other adventitious sounds could be heard. Examination of the lungs, the central nervous system, and the urine yielded no abnormal findings.

Some condition simulating coronary thrombosis that could explain these signs and symptoms was sought and dissecting aneurysm of the aorta seemed a possibility. The radial pulses on the two sides were found different in strength and confirmation was obtained by the sphygmomanometric reading of of 80/? on the right and 120/? on the left. The dorsalis pedis and posterior tibial arteries were easily felt in both legs and found of equal volume. A slight transient " peculiar " feeling in his head was later mentioned by the patient to have preceded the onset of the severe pain in the infra-umbilical region by a short while.

Another finding that came to notice later was a difference between the right and left carotid pulsations. They were reduplicated on the right and single on the left, without a coexisting noticeable difference in the intensity of the pulsations on the two sides. There were two almost equal beats in quick succession on the right carotid for every single beat on the left. The right radial pulse, however, like the left, was single but weaker. Electrocardiography could not be carried out owing to an unfortunate breakdown of the apparatus.

The same evening, the pulse rate dropped to 36, although his general condition was improved. The next day it went up to about 55 a minute. Towards the evening the patient developed an acute exacerbation of the symptoms and of the abdominal signs—excruciating epigastric pain radiating below the umbilicus and upwards into the lower chest, with guarding that almost amounted to rigidity. About an hour later he gave a few gasping breaths and died suddenly.

Necropsy (Dr. A. J. McCall). The body was that of a rather emaciated man.

Skull and brain. These were not examined.

Thorax. There was a hæmopericardium with 600 g. of recent blood clot closely investing the heart. The aorta showed a 2·5 cm. horizontal tear about 4 cm. above the aortic ring. At right angles to this and running into it was a longitudinal tear, which had curled round beneath the adventitia. In one place, the adventitia had given way, giving rise to the hæmopericardium. Blood had spread beneath the epicardium and into the auricular septum where hæmorrhages were present in close relation to the A-V bundle. Distally, the blood had dissected the aorta down to the fourth lumbar vertebra, where a second tear allowed re-entry into the aorta. Dissection had occurred along the innominate artery, but not along the left subclavian or left carotid arteries, so that the difference in blood pressure during life on the two sides was explained. The aorta at the site of the rupture was thinned but not otherwise obviously abnormal. Distally, however, there was much atheroma and some pearly intimal thickening.

Heart. This was not unduly large. The coronary arteries showed only slight atheroma.

Abdomen. Some blood had effused behind the peritoneum in front of the pancreas and in its substance. The spleen was slightly enlarged and firm. The abdominal organs were otherwise healthy.

Discussion

Clearly the terminal event causing the sudden death was the rupture into the pericardial sac, with a consequent hæmopericardium and tamponade. The partial heart block could be explained by the blood seeping into the auricular septum and across the A-V bundle, and the low abdominal pain by extension of the dissection as far down as the fourth lumbar vertebra, but why the pain was first manifest there was not clear. The severe epigastric pain simulating an acute abdominal emergency seems to be best explained by the hæmorrhage in front of and in the substance of the pancreas.

The only single diagnosis to explain the multiplicity of signs and symptoms seemed that of dissecting aneurysm of the aorta. In the absence of pathognomonic signs, however, the suspicious past history of the patient with a double retrospective diagnosis of peptic ulcer and angina pectoris, and the obvious abdominal signs including release tenderness, especially for the first few hours, combined to make the consideration of other conditions in the differential diagnosis seem necessary.

Cardiac infarction seemed unlikely and syphilitic aneurysm of the upper aorta could cause the pain in the lower chest and the difference in the brachial blood pressure, but other corroborative signs were missing. Acute abdominal conditions could not explain the brachial difference in blood pressure and the partial heart block, but it was thought that they might

supervene in a case that had those signs already from preceding hypertension, arteriosclerosis, and myocardial degeneration. Not long before, a patient suspected of having aortic aneurysm because of a difference in brachial blood pressure of 30 mm. was shown at necropsy to have bronchial carcinoma and a deformed right clavicle.

Even after dismissing the cardiac signs as coincidental, any of the abdominal conditions thought of seemed to leave a great deal unexplained. Mesenteric embolism lacked its usual abdominal distension, colicky obstructive type of pain, and nausea and vomiting. Acute pancreatitis was more seriously considered, but the onset seemed rather too sudden and still did not explain the initial low pain. Perforation of a peptic ulcer lacked its board-like rigidity and restriction of abdominal mobility with respiration. The subsidence of the abdominal pain without the supervention of a peritonitic stage at the time of re-examination by the surgeon seemed almost to rule it out.

It is interesting to note what Shennan wrote regarding the course of the pain. " In some cases a very characteristic feature which gives an important clue to the condition present is the gradual disappearance of the pain, the relief persists for hours or days or even a week or two, but the pain recurs later with similar rapidity and rapid death." Although the relief in this case was far from complete, the sequence of events seems to be very similar.

The clinical manifestations of dissecting aneurysm of the aorta are protean. Simple meditation on the anatomical aspects would soon conjure up an almost endless chain of symptoms, signs, and differential diagnoses. It is the coexistence of certain groups of signs and symptoms rather than any single one of them that should almost always lead one to suspect the condition. Sometimes, however, it is a long way from making certain of the diagnosis.

Among the leading symptoms of this catastrophe, the pain with its type, mode of onset, and distribution is of paramount importance in diagnosis. It is usually very severe, extremely sudden, and is described as splitting, tearing, rending, crushing, or knife-like in character. As a rule, it is felt in the midthorax, front or back, and usually descending from above downwards. It may be felt in the neck, mandible, head, beneath the left or right scapula, in the shoulders, lumbar regions, loins, epigastrium, right or left hypochondrium, right or left iliac fossa, and infra-umbilical region. It may also radiate into the legs, as far down as the toes, but radiation into the arms is unusual. Typical coronary thrombosis pain has also been described from extension of the dissection into the ostia of the coronary arteries. Sweating, faintness, shock, and collapse are frequent and may be extreme. Palpitation from extrasystoles or ventricular tachycardia may be complained of. Dyspnœa is frequently reported and appears to be more pronounced than is generally realized; it may be severe and lead to orthopnœa. Another important group of symptoms is due to the dissection extending along the peripheral vessels: along the external iliacs producing numbness, coldness, and weakness of the legs; along the coeliac axis or mesenteric vessels producing nausea and vomiting, diarrhœa, hæmatemesis, melæna, abdominal cramps, or distension; or along the renal vessels, producing hæmaturia and anuria. Even subcutaneous hæmatomata have been recorded, from dissection of the superficial vessels. Involvement of the cerebral arteries can result in a whole gamut of symptoms from headache to coma: visual disturbances, facial paralysis, loss of speech, hemiplegia, paraplegia, visceral pains of tabetic type, and incontinence. A third variegated group may be met with from rupture of the dissecting aneurysm anywhere inside the chest, and from pressure effects so produced: cough, sensation of suffocation, dysphagia, hoarseness, and hæmoptysis. Symptomless cases are known to occur.

A sign has been met with in the present case to which no reference could be found. This was the unilateral reduplicated beat of the carotid artery. The explanation must lie in the difference of the rate of propagation of the pulse wave through the lumen of the artery and through its dissected coats where the blood was probably partly clotted. At necropsy, this was the only pathological finding that could account for it. The full significance of this sign was not realized until then. White (1944) in his authoritative summary of dissecting aneurysms says, " There are no pathognomonic signs of dissecting aneurysms." Since, however, there does not seem to be any other pathology that could produce this unilateral double beat in an artery, its pathognomonic significance is at once appreciated. The frequency and usefulness of this sign may be greater than is at present realized, and it may occur in other arteries. Looking for this sign by palpation of all accessible arteries may reveal further instances.

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Two other signs of dissecting aneurysm have been added in recent years. Roesler, Gifford, and Betts (1937) described the appearance of a rapidly shifting area of pulsation in the interscapular area, over which the aortic second sound was very accentuated: it was also associated with a rapid change in the radiological appearance of the aortic shadow. The other sign was due to Logue (1943) and consisted of a bruit and a thrill over the femoral artery.

Delay in the conduction of pulse beats is also significant. " In dissecting aneurysm of the aorta delay of the pulse beat, when compared with the apical beat, can occur in all arteries, resulting from delay and weakening of the blood stream entering or passing through the involved artery or arteries " (Shennan, 1934). Appreciable help may be obtained from the search for these simple signs in suspected cases.

Summary

A review of the improved diagnosis of dissecting aneurysm of the aorta during life is presented. Its manifestations are protean, but some leading symptoms are singled out.

A case in which this diagnosis was considered as the only one to include all the signs and symptoms under a single pathology is described.

A new sign of this disease is described consisting of unilateral reduplicated arterial pulsation, in this case in the right carotid artery. Its pathognomonic significance is discussed, and other recently described signs are reviewed.

I should like to render my thanks to Dr. A. Wilson Gill for his help and Dr. A. J. McCall for the use of the post-mortem report

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ANEURYSMAL DILATATION OF THE LEFT AURICLE WITH EROSION OF THE SPINE

BY

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Received May 19, 1946

Although aneurysmal dilatation of the left auricle, due to mitral stenosis, is not uncommon, the following case is unusual for the enlarged auricle eroded the vertebral column, causing severe pain in the right chest, and became adherent to the right chest wall, leading to systolic retraction in the right axilla.

Case Record

In August, 1945, a single woman, aged 38, employed in clerical work, was admitted to the Manchester Royal Infirmary, under the care of Dr. Crighton Bramwell, on account of severe pain in the right chest of four years' duration. Apart from scarlet fever and an antral operation in childhood, her health had been good until the age of 22 when she developed rheumatic fever and was treated in hospital for five months. She was subsequently troubled by occasional faintness and palpitation but carried on her occupation as a clerk, with little time off work owing to ill-health, until the age of 26 when she had an attack of lobar pneumonia. She never again resumed her occupation and became unable to undertake household duties owing

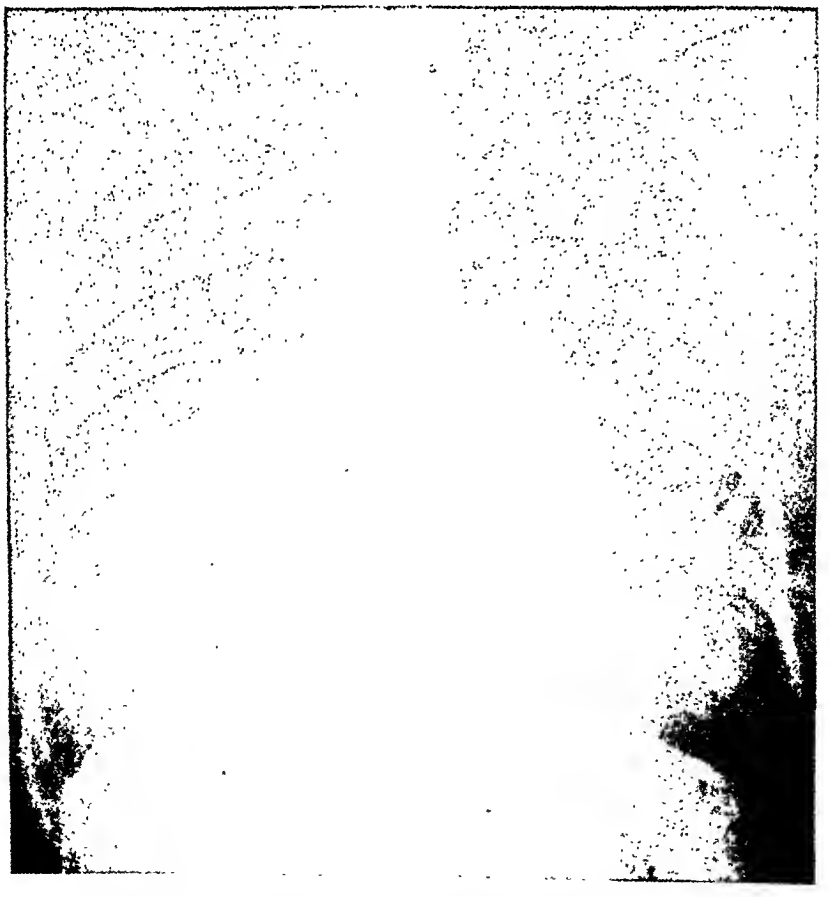


Fig. 1.—Teleradiogram, 1943. Anterior view, showing great dilatation of left auricle to the right.

to severe dyspnoea on exertion. Aged 34, she began to suffer from gripping pain starting at the inferior angle of the right scapula and radiating round the chest to the right axilla. This occurred on exertion, on swallowing, or when her stomach was distended with food, and was relieved by rest and sometimes by alkalis. In July 1943, when aged 36, she was seen by Dr. Bramwell on account of this pain, and was found to be suffering from severe mitral stenosis with gross cardiac enlargement and uncontrolled auricular fibrillation. On cardioscopy, the left auricle was grossly dilated (Fig. 1 and 2). She was admitted to the Manchester Royal Infirmary,

FIG. 2.—Right anterior (I) oblique radiogram, 1943, showing displacement of barium filled oesophagus by left auricle.

under Dr. Bramwell, and was given digitalis with improvement in her capacity for exertion. She remained under our observation, with persistent fibrillation, and, apart from the pain, relatively well, until August, 1945, when she was readmitted to hospital because her pain, hitherto tolerable, had become very severe and almost continuous, being no longer relieved by rest. A cardiogram six days before admission showed auricular fibrillation with right axis deviation (Fig. 3A).

On examination she was much wasted, and distressed by pain. The pulse was completely irregular, rate 136 a minute; blood pressure 130/90 mm. The heart was enlarged; at the apex a very loud first sound and a long rumbling diastolic murmur were heard. There was no evidence of right ventricular failure. The right lower chest was dull on percussion and breath sounds and tactile fremitus were almost absent; moist sounds were present at both lung bases. Systolic retraction was conspicuous in the sixth, seventh, and eighth intercostal spaces in the right mid-axillary line. On cardioscopy the heart was grossly enlarged and the right lower chest was radio-opaque. Right oblique and lateral views failed to show any erosion of the spine; unfortunately left oblique views were not taken.

Two days after admission normal rhythm with a prolonged P–R interval was recorded (Fig. 3B) and, apart from several attacks of regular tachycardia (Fig. 3C) lasting some hours,

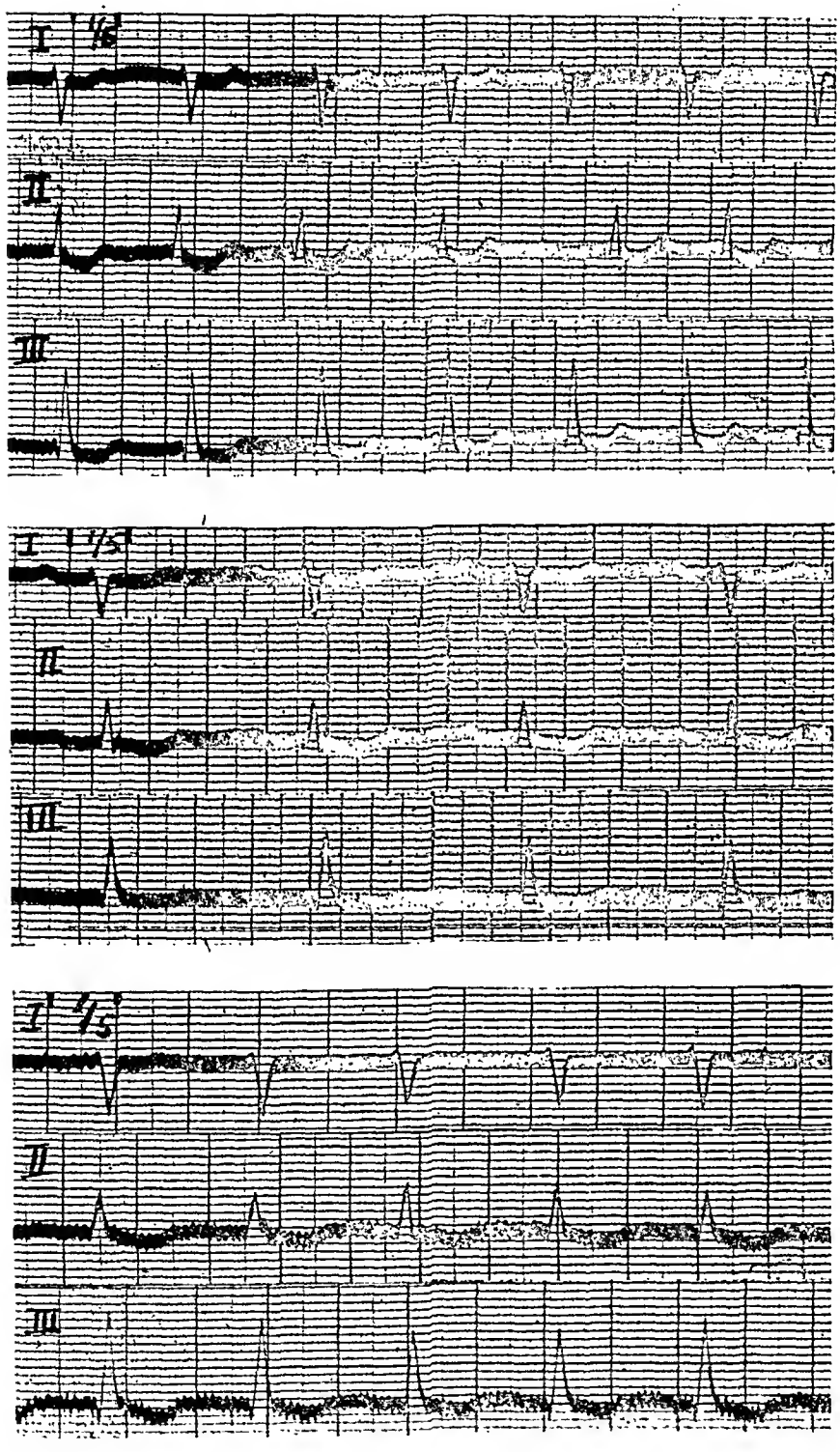


FIG. 3.—(A) Cardiogram six days before admission, showing auricular fibrillation with right axis deviation and digitalis effect.
(B) Cardiogram two days after admission, showing sinus rhythm with a prolonged P–R interval.
(C) Cardiogram during an attack of regular tachycardia, rate 140 a minute. (Calibration: $3mV$= 2 cm.)

this persisted until her death seven weeks later. In spite of treatment her condition gradually deteriorated; she became more feeble and wasted, and her pain increased in severity, being relieved only for short periods by full doses of morphia. Two days before death slight oedema of the legs appeared, but there was no gross right ventricular failure.

Necropsy was performed by Dr. F. A. Langley, 23 hours after death. The heart weighed

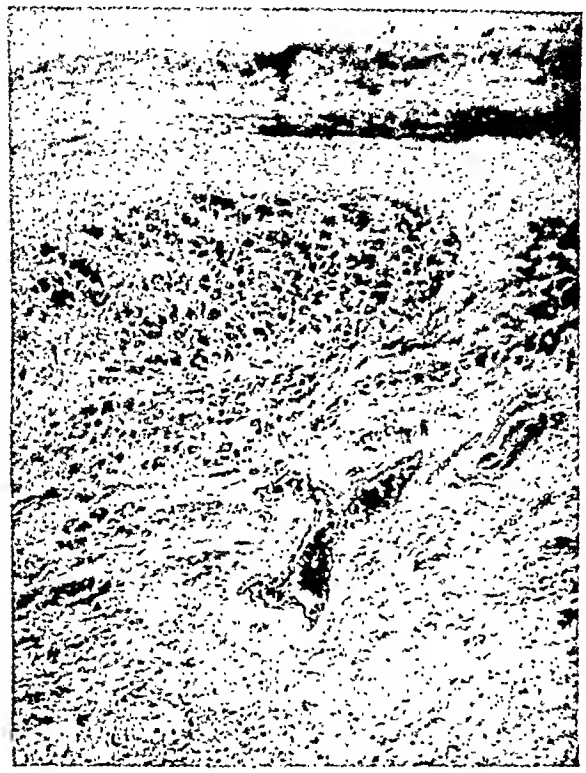
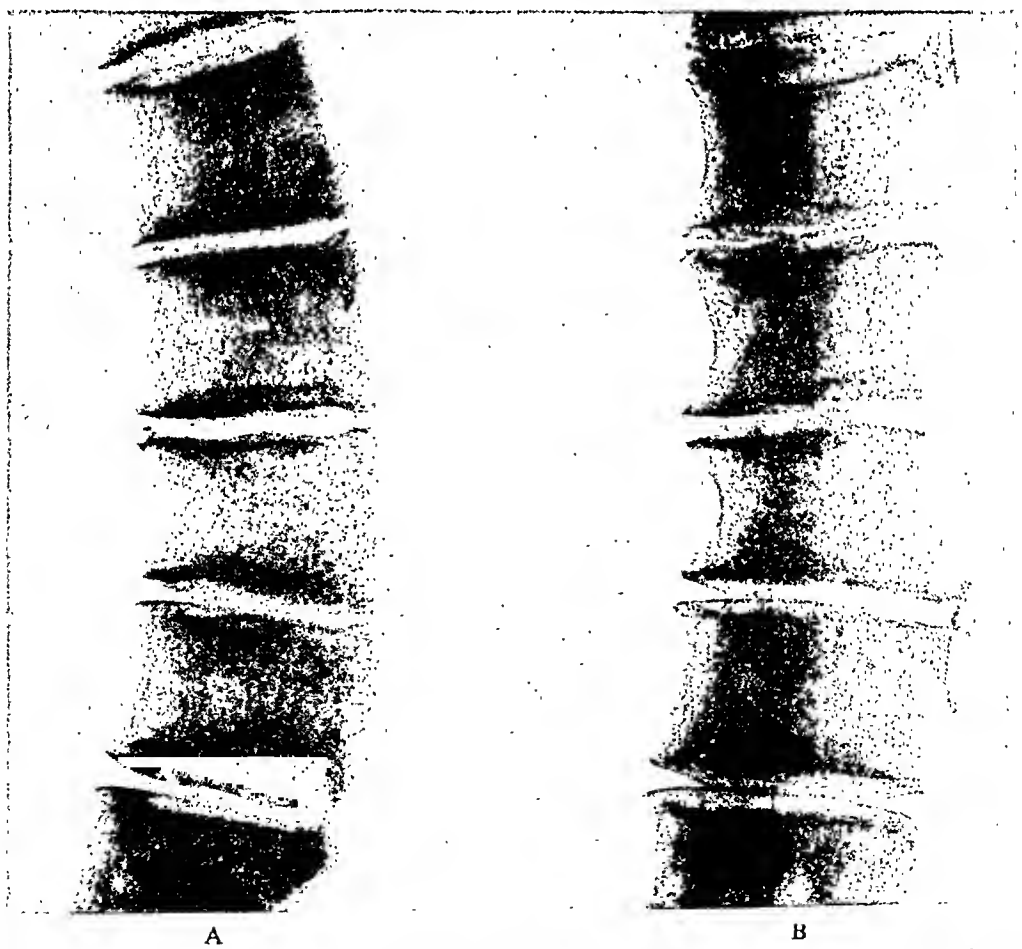


FIG. 4.—Section of left auricular wall stained with haemalum and eosin. Although there is some fibrosis, a considerable number of muscle fibre bundles can be seen. Magnification: ×36.



A B

FIG. 5.—Post-mortem radiograms of the dorsal spine. (A) Lateral view which fails to show the erosion. (B) Left anterior oblique view showing erosion of the right antero-lateral aspects of the vertebral bodies. The deeply eroded vertebra is the seventh dorsal.

420 g. The right border, formed by the left auricle, extended 10 cm. to the right of the midline. The lower lobe of the right lung was partially collapsed and firmly adherent to the chest wall laterally and to the pericardium and left auricle medially. The left auricle was enormously dilated and its wall thin; microscopy of the wall revealed some fibrosis, but a considerable amount of muscle tissue was present (Fig. 4). The right auricle was moderately dilated; the right ventricle was 3–4 mm. in thickness. The left ventricle was moderately dilated, the wall measuring 1 cm. in thickness. The mitral valve was severely stenosed and reduced to a narrow slit 1·5 cm. in length; the tricuspid valve was slightly stenosed (circumference 10·5 cm.) and its cusps and chordæ tendinæ were thickened. The aortic cusps were slightly thickened; the pulmonary valve appeared healthy. The fifth, sixth, seventh, eighth, and ninth thoracic vertebral bodies were eroded, the intervertebral discs being spared. The erosion of the seventh vertebra was most conspicuous (Fig. 5). Apart from some chronic venous congestion, the remaining organs were healthy.

Discussion

Erosion of the spine by a dilated pulsating auricle lying against it does not seem surprising, but we have been unable to find any report of a similar case. Since importance has been attached to pulsation as a factor in the mechanism of erosion of bone by arterial aneurysms, it is interesting that a fibrillating auricle should be capable of similar erosion. It is tempting to suggest that reversion of the auricle to normal rhythm played a part in the exacerbation of the pain in the later stages. The presence of vertebral erosion combined with the distribution of pain strongly suggested root pressure, which would explain the intractable character of the pain. Had this possibility occurred to us during life, paravertebral root injection might have been tried, for there seems little doubt that the severe continuous pain played an important part in the progressive deterioration of the patient's condition that ultimately led to death. In the earlier stages pain was provoked by exertion and relieved by rest. It is possible that the rise of venous pressure during exertion, by further distending the auricle, increased root pressure, and that the fall in auricular pressure with rest reduced it. Pain in the right chest on exertion in a case of aneurysmal dilatation of the left auricle was described by Bedford (1927) but necropsy findings were not available. Systolic pulsation on the right side of the chest has been recorded by Dressler (1937) and by Bedford (1927) but we have not found a case in which systolic retraction was noted.

It seems surprising that, after years of fibrillation, the enormously dilated left auricle should have been capable of reverting spontaneously to normal rhythm. We have, however, seen normal rhythm return in a case of greatly dilated left auricle in which fibrillation had persisted for 19 years; but in that case fibrillation recurred within a week. The amount of muscle tissue in the auricular wall in the present case was much greater than that usually found in an extremely dilated left auricle and this may have facilitated reversion to normal rhythm.

Summary

A case of aneurysmal dilatation of the left auricle associated with mitral stenosis is described in which severe pain in the chest was a prominent symptom. Necropsy showed erosion of the bodies of several dorsal vertebrae, due to pressure from the dilated auricle. Systolic retraction of the chest wall in the right axilla and spontaneous reversion to normal rhythm after fibrillation had persisted for several years were other unusual features of the case.

We are indebted to Professor Crighton Bramwell for permission to publish details of this case, to Dr. E. Duff Gray for the clinical radiograms, to Dr. F. A. Langley for his help with the pathology, and to Mr. F. Ward for the post-mortem radiograms and the microphotograph.

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EARLY DIAGNOSIS OF RHEUMATIC VALVULAR DISEASE IN RECRUITS

BY

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Received September 25, 1946

During the world war of 1939–45 the call for men for the armed forces made the medical examination of potential recruits an important field of medical service, and many were rejected for heart disease. The major problem for cardiologists was to detect the presence of rheumatic heart disease when it was early and symptomless, a stage not seen except incidentally in peace-time practice. It might at first be thought that with the advent of peace the importance of very early diagnosis would quickly fall. But it is becoming evident that in economic and labour conditions after this war, comparable medical examinations will be multiplied and that in time few employees will be accepted without them.

From 1940 to 1945, 2500 men suspected of cardiac abnormalities were referred to one of us (J. P.) by medical boards. Among them were found 609 cases of early rheumatic heart disease, of which only a quarter had symptoms, and those slight. Only 264 had mitral valvular disease, a low proportion due to the fact that mitral stenosis is more easily identified by medical boards than aortic incompetence, and that those with mitral disease more often get symptoms at an earlier age and, therefore, come under medical observation. It is on the analysis and study of these 609 together with a limited survey of the literature, that this paper is mainly based. Table I shows the relative incidence of various cardiovascular defects. Cases of effort syndrome (neuro-circulatory asthenia) were not included.

TABLE I

CARDIOVASCULAR DISEASE AMONG 2500 MEN REFERRED BY MEDICAL BOARDS

Rheumatic heart disease	609	(76 per cent)
Congenital heart disease	71	(9 per cent)
*Hypertension	49	(6 per cent)
Enlargement, cause unknown	25	(3 per cent)
*Hyperthyroidism	12	
Angina of effort	12	
Coronary thrombosis	5	
Syphilitic aortic incompetence	4	
Parox. tachycardia	10	
Bundle branch block	2	
Complete heart block	1	
Auricular fibrillation	5	
Auricular flutter	1	
	806	

* These figures are smaller than might be expected because many such cases were referred to physicians other than cardiologists.

The figures in Table I may be compared with those given in a table shown among the individual reports of the chairmen of the special medical advisory boards in the United States (Fenn *et al.*, 1944). Of 698 rejected for cardiovascular disease and disorder, 396 had rheumatic heart disease, 43 had congenital heart disease, and 161 had hypertension; neuro-circulatory asthenia accounted for 61 rejections.

The proportion of cardiovascular disease among recruits in this country has been given as

9 per cent of 30,000 rejections for all causes ; of this 9 per cent, four-fifths were for rheumatic heart disease (Parkinson, 1945). In the United States, Rowntree (1945) estimated that 6 per cent of 2,976,000 total rejections were for cardiovascular reasons. About half were due to rheumatic lesions (Levy, Stroud, and White, 1943). Wilburne and Ceccolini (1944) examined 20,000 men and found that 6 per cent of all rejections were for cardiovascular lesions and that 63 per cent of these were rheumatic. Perrot (1944) found that 8 per cent of all rejections were for cardiovascular reasons.

Method of Examination

Past History. No great reliance was placed upon a past history of rheumatic fever or chorea, whether negative or positive; too many men, in their eagerness to serve or to escape service, will falsify such a history; the same applies to a story of dyspnœa on exertion.

Inspection. This served to exclude obvious anæmia or goitre, and to note nutrition, physique, and any deformity of the chest or spine.

Palpation. The apex beat was then found by placing the whole hand lightly upon the chest wall under the left breast. It was noted whether the impulse was displaced or too forcible. Minor degrees of scoliosis frequently move the apex beat outwards. The anterior chest wall was then palpated for the presence of a thrill, the palm of the hand being laid lightly over the apex and then over the base of the heart. A thrill at the base of the heart may best be felt by the observer standing on the right of the subject who leans forward and stops breathing at the end of full expiration ; the hand should be merely applied to the chest wall, not pressed hard. No reliance whatever was placed upon a doubtful thrill at any site.

Auscultation. The heart sounds were then considered, whether normal or abnormal, their loudness, and any variations in character which frequently lead to doubt in diagnosis. A split first sound which is fairly common in health sometimes led to an unjustified suspicion that early mitral stenosis was present; an accompanying double quality in the feel of the apex beat added to this suspicion. The first sound may otherwise vary in loudness or clarity in different subjects without significance. It is often said that a pulmonary second sound, loud or duplicated or both, is a sign of early mitral disease. But this is not so—such variations are common in healthy young adults. The normal third heart sound, so common in the young (Thayer, 1909 ; Evans, 1942*b*), was also frequently mistaken for a mitral diastolic murmur. Bramwell (1943) found a reduplication of the second sound at the apex, which he considers to be identical with the third heart sound, to be frequently mistaken for mitral stenosis.

Murmurs were first considered with the subject standing, then when lying; and again when in the left lateral position after exercise. During this procedure a presystolic murmur is heard best at the higher range of rate, and an aortic diastolic during the lower range of rate. We have found it convenient thus to listen for an aortic diastolic murmur on the left of the sternum while the heart rate is falling after the subject has exercised and turned half over on his left side, and immediately after deciding on the presence or absence of a presystolic murmur at the apex. The aortic diastolic murmur is also well heard with the subject leaning forward with the breath held at the end of full expiration. We have often been exhorted to keep an *open* mind, and in general this is sound advice. We do naturally listen without preconceived ideas of what will be heard; and we cannot help noticing a first sound which is unusually loud or when there is an obvious systolic murmur. That is easy, and now comes the moment to *close* the mind to what is likely to preoccupy it and to concentrate upon answers to special questions :

(1) Is there a mid-diastolic murmur at the apex, a distant murmur beginning with the third heart sound but distinguishable from it ? If so there is mitral stenosis. (2) Is there a diastolic murmur immediately following the second sound? If so there is aortic incompetence and the murmur can be tracked up the left border of the sternum to its aortic source. Murmurs were timed by the carotid pulse, felt best with the observer's left hand resting on the right side of the patient's neck, the thumb on the artery.

The Pulse. The rate and rhythm of the pulse were noted at the end of the examination, when the recruit was more composed. Its response in rate to effort was noted when auscultating after exercise, but no so-called exercise tolerance tests were made.

Radioscopy. Radioscopy was used in every case, employing the three standard positions, i.e. anterior, right oblique, and left oblique ; and all statements on heart size were based on radioscopy, occasionally supported by teleradiography.

Electrocardiography. Cardiograms were taken on the first 500 cases but their value was so limited that subsequently they were taken only for extra evidence when diagnosis was difficult or when an unusual rhythm was present. This agrees with the conclusions of Wood, Wolferth, and Miller (1941) based on a large experience. The exigencies of war practice had also to be considered. But a cardiogram was always taken in suspected myocardial disease, chiefly among the older recruits.

The Diagnosis of Early Mitral Valvular Disease

This entails a discussion of the significance of the apical systolic murmur which has been regarded as the commonest murmur in mitral stenosis (Graham Steell, 1906). We doubt whether this is true of young adults judged by our experience with recruits. Of 184 recruits diagnosed certainly as mitral stenosis, 104 had a presystolic murmur (in 72 alone, in 3 with a diastolic, and in 29 with a systolic murmur in addition) ; 13 had a mitral diastolic murmur only; 5 a loud apical first sound only; and 2 were diagnosed solely on the X-ray appearances, there being no abnormal auscultatory sounds. A further 60 had only a systolic murmur. One might expect to find in current textbooks, under mitral stenosis and its diagnosis, a special reference to the first signs permitting its early diagnosis ; but the description is usually that of the fully developed disease as seen in patients with symptoms seeking medical advice. In contrast, war requires, and peace should require, the recognition of the symptomless valve lesion.

The Apical Systolic Murmur. The commonest cause for a medical board to want a cardiologist's opinion was the presence of an apical systolic murmur. If it was not overlooked, the common soft pulmonary systolic murmur was apparently more easily assessed as insignificant.

We have reserved the term incidental—preferring it to the term functional—for those systolic murmurs that occur not only in health and, therefore, could be classed as innocent, but also in anæmia and pyrexia—murmurs that are not indicative of cardiovascular disease. Systolic murmurs also occur with " relative incompetence " of the mitral valve, as in association with aortic incompetence or stenosis, in hypertension, rheumatic carditis, subacute bacterial endocarditis, and heart failure. Rheumatic heart disease affecting the mitral valve is a third and the most important source of this sign. A harsh systolic murmur with thrill near the sternum in the fourth or fifth left interspace may be congenital—that of a ventricular septal defect.

The incidence of systolic murmurs in any group of apparently healthy people is high. Contratto (1943) heard such murmurs in 350 (12 per cent) of 2856 college students examined ; of these, 208 were classed as functional, 9 as rheumatic valvular disease, 6 as congenital lesions and 127 were regarded as more than functional, though the physical signs were insufficient to permit an exact diagnosis. Wilburne and Ceccolini (1944) found 297 functional murmurs among 20,000 recruits. In our own series 259 (10 per cent) incidental murmurs of impressive intensity were heard.

Studies of the natural history of the systolic murmur such as those by Blumenthal (1942) and by Baker, Sprague, and White (1943) underline the great difference in prognosis between the incidental (or functional) murmur and the organic mitral systolic murmur. The difficulties in the assessment of the systolic murmur are considerable; Master (1944) asserted that many men admitted to the U.S. Navy with so-called functional murmurs were later boarded out with valve lesions.

Incidental murmurs are generally soft and short, and they vary in intensity both with position and with respiration to a greater degree than organic murmurs. They are unaccompanied by symptoms or signs of heart disease. Radioscopy shows a heart normal in shape and size. There may be some chest abnormality such as a depressed sternum which is often associated with a systolic murmur, an association noted twelve times among our 2500 recruits. The term " cardio-respiratory " applies by definition to systolic murmurs varying with respiration, disappearing at some phase, often that of full expiration or inspiration. In practice

they are short and soft, and seldom present difficulty. Exocardial murmurs were heard in three men. Scadding and Wood (1939) have drawn attention to a systolic click that occurs in cases of left-sided early pneumothorax.

The important features in assessing a systolic murmur are loudness and length, the presence or absence of a diastolic murmur, and evidence of enlargement of the heart on X-ray. As regards the intensity, White (1927) showed that there is a distinct difference in prognosis between the three groups of loud, moderate, and slight murmurs. Levine (1933) and Freeman and Levine (1933) advised that systolic murmurs be graded into six groups according to their intensity: they found that only the first two groups of this classification were of no significance and that the majority of functional murmurs fell into the first group, which consisted of the very shortest and softest murmurs.

Evans (1942*a*) has lately again stressed the importance of the late systolic murmur, i.e. a murmur occurring late in systole, separated from the first heart sound by a short interval; although this murmur is often noticeable, Evans believes that it is always innocent. Twenty-four such murmurs were heard among the 2500 recruits seen, and there was never any reason to think they represented mitral disease. A medical board, however, might regard them as evidence of mitral stenosis or of aortic valvular disease (Table II).

TABLE II

ANALYSIS OF THE DESCRIPTION OF 24 "LATE SYSTOLIC MURMURS" AS STATED BY MEDICAL BOARDS WHEN SEEKING A CARDIOLOGIST'S OPINION

(1) Systolic murmur at the apex	7
(2) No reference to the murmur	3
(3) Apical murmur with no reference to timing	4
(4) Diastolic murmur	4
(5) Presystolic murmur	2
(6) Systolic and diastolic murmurs	2
(7) Board stated difficulty in timing the murmur	2
	24

The intensity of murmurs may be graded simply into three groups, soft, moderate, and loud, and the length may be given as short, moderate, or long. The phrase "the murmur replaces the first sound" used often to be employed, but now it is assumed that if the systolic murmur is long and loud enough the first sound may be ousted. The conduction of a murmur is little more than a measure of its intensity (Levine and Likoff, 1944). We join with Levine (1933) and Freeman and Levine (1933) and Bramwell (1942) in hesitating to call a loud systolic murmur incidental or functional, even in the absence of collateral signs of heart disease. It is in such cases that the routine use of the phonocardiograph may be of great use in the near future. Whether a recruit should be accepted for the forces when he possesses a very noticeable but innocent systolic murmur is open to argument. We think that unless extremely keen, such a man runs the risk of a "doctor made" cardiac neurosis (Hill and Dewar, 1945). Some claim that this is placing the individual before the State, but such a soldier may become more of a liability than an asset in any active unit.

MITRAL STENOSIS WITH A PRESYSTOLIC MURMUR

One hundred and four (almost 40 per cent of all the cases of mitral valvular disease) cases of mitral stenosis with a presystolic murmur, and all with a loud first sound, were seen. Of these 37 per cent gave a history of rheumatic fever, 15 per cent of chorea, and 3 per cent of both (total 55 per cent). Among men without heart disease a history of rheumatic fever was given in 14 per cent, of chorea in 2 per cent, and of both in 0·1 per cent, a total of 16 per cent. This figure is higher than in the normal population because such histories often influenced the medical boards in deciding to seek a cardiologist's opinion. More reliable percentage frequency of rheumatic history in the normal is that of 1000 men studied during the first world war, namely 5 per cent (Parkinson, 1945).

Dyspnœa on exertion was the only symptom considered; in all cases of mitral stenosis, no matter what the physical signs, the proportion with dyspnœa proved to be about the same, 20 per cent. Short-windedness must always be considered in relation to the build, occupation,

and condition of the patient. Many men with mitral stenosis showed a loud and sudden first sound as the only obvious physical sign. In the majority, however, a presystolic murmur was evoked by exertion and then heard in the left lateral position. In the absence of a presystolic murmur, and in the absence of tachycardia, the characteristic apical first sound points to the probability, but not the certainty of mitral stenosis. Other causes of a loud first sound are hypertension, tachycardia, and thyrotoxicosis, and in the last especially it can resemble a presystolic murmur. In five cases with a loud and sudden first sound only, and tachycardia absent, exertion failed to elicit a presystolic murmur; yet the X-ray appearance was, in all five, diagnostic of mitral stenosis. Thirteen cases had a mitral diastolic murmur only, limited to the apex. The percentage having symptoms was essentially the same in this last group as in those with a presystolic murmur; the percentage with a positive rheumatic history was also identical with that of the presystolic group.

TABLE III

AUSCULTATORY SIGNS IN 184 CASES OF EARLY MITRAL STENOSIS

Presystolic murmur only	72
Presystolic murmur and systolic murmur	29
Presystolic and diastolic murmur	3
Loud mitral first sound only	5
Diastolic murmur only	13
Systolic murmur only	60
No abnormal auscultatory signs	2
	184

MITRAL STENOSIS WITH A MURMUR, SYSTOLIC NOT PRESYSTOLIC

In a total of 264 cases seen with mitral valvular lesions, 60 had a mitral systolic murmur of moderate or loud intensity and of moderate or long duration. This with a combination of an apical systolic thrill in 9 ; a rheumatic history in 48 per cent, chorea in 7 per cent, and both in 5 per cent (total 60 per cent) ; dyspnœa on exertion ; and a loud first sound, or X-ray changes (90 per cent), allowed a diagnosis of mitral stenosis to be made with some certainty.

MITRAL INCOMPETENCE

Between the two world wars it was frequently taught that mitral incompetence was rare, and incidental (or functional) murmurs were diagnosed freely. A mitral lesion without stenosis is not commonly seen at necropsy. Cabot (1926) found only seven cases of mitral incompetence in 4000 autopsies, and three of these he thought were doubtful. Cabot followed many cases of the classical triad of apical systolic murmur, loud pulmonary second sound, and an enlarged heart, but post-mortem there was rarely evidence of mitral incompetence without mitral stenosis. Mackenzie (1925) held almost similar views and regarded mitral stenosis as the essential rheumatic valvular lesion. On the other hand, de la Chapelle, Graef, and Rottino (1934) record the necropsy findings in 7 cases of mitral incompetence. Of 100 necropsies reported by Bland, White, and Jones (1935) on patients dying from rheumatic heart disease below the age of 21, 25 had valve deformity without stenosis: of these 100 cases, recrudescence of the rheumatic infection was directly responsible for 85 deaths. Dana and Reidy (1936) graded 150 cases of mitral disease at the post-mortem examination; pure mitral incompetence was not uncommon, forming in fact one-fifth to one-half of all cases; and the writers expressed the belief that this condition can by itself cause death. Levine (1945) believes that mitral incompetence is occasionally found post-mortem; he reports cases with apical systolic murmurs and subsequent bacterial endocarditis where post-mortem a pure incompetence of the mitral valve is found. Bourne (1946) has recently recorded the necropsy findings in such a case. It seems that pure mitral incompetence though uncommon does occur especially in the young, and proceeds to stenosis later, so that it is rarely seen without it after the age of twenty.

Twelve cases were seen in which doubtless there was mitral disease, but in which the evidence was insufficient to warrant the diagnosis of mitral stenosis. These were labelled mitral incompetence (rheumatic). All had an apical systolic murmur, 6 had a positive rheumatic history, 5 showed slight general enlargement on radioscopy, and 2 others slight enlargement of the left ventricle. Other and almost identical cases as regards signs (described above) were classed as mitral stenosis, mainly because of X-ray evidence.

A greater problem was presented by as many as 68 subjects (25 per cent of the whole group of mitral valvular disease) classed as " probable mitral valvular disease (mitral incompetence)." The alternative diagnosis was a healthy heart with a noticeable but incidental systolic murmur. An apology is perhaps necessary for the size of this group ; for in military practice it may be politic to exclude all who carry so suspicious a murmur lest later they should fall sick or claim unjustifiably a pension. In civilian life they might have been recorded as " For observation, ? organic heart disease" and would then have been followed up over a period of months or years. Here also phonocardiography will, in future, prove invaluable. Of this group, 45 gave a positive and circumstantial history of rheumatic fever or chorea in youth. Dyspnœa was claimed by 14, and 1 gave a history of hæmoptysis. A systolic murmur at the apex was heard in 45, varying from soft to moderate in intensity and short to moderate in length. In 24 of them the apical first sound was loud and sudden. In 9 doubt existed as to the presence of a mitral diastolic murmur. Of these cases 30 showed a doubtful or borderline enlargement of the left auricle in the right oblique position; in 8 the heart seemed to be generally though slightly enlarged; in 4 the cardiogram showed right axis deviation.

TABLE IV

CASES THOUGHT TO HAVE MITRAL VALVULAR DISEASE

Mitral stenosis	184
Mitral incompetence	12
Mitral valvular disease probable	68
	264

Mitral stenosis without murmur. In two cases the diagnosis rested on the radiological appearance alone. In one, auricular fibrillation was present and the heart was enlarged (X-ray), the size of the left auricle being diagnostic. The other case had tachycardia, and here the left auricle and the conus were both enlarged. Sosman (1940) has termed this variety the " sub-clinical type."

RADIOSCOPY IN MITRAL VALVULAR DISEASE

The difficulties of clinical diagnosis of mitral valvular disease have been reduced by the use of X-rays. In such inspections it is important to bear in mind the influence of the position of the diaphragm on the cardiac shadow. Just as a high diaphragm by raising the heart and rotating it may give an appearance similar to that of mitral stenosis, so a low diaphragm may conceal the minor changes to be expected in mitral disease.

Our radioscopic findings show no significant difference between the cardiac outline of mitral stenosis in those with a presystolic murmur and in those with a systolic murmur only. Among those with a presystolic murmur only, 104 in all, enlargement of the left auricle was the only certain X-ray change in 77 (74 per cent) ; in 13 the pulmonary artery and the conus were also enlarged; in a further 14 (13 per cent) there was no change in the size or shape of the heart. Of those with a diastolic murmur, 13 in all, 6 cases had a large left auricle, 4 enlarged pulmonary artery and conus; and 3 showed no change. Of those with an apical systolic murmur and mitral stenosis (60 in all), 40 (67 per cent) had left auricular enlargement, 14 had enlargement of the pulmonary artery and the conus, and a further 6 (10 per cent) showed no change. Thus about 10 per cent of cases of early mitral stenosis show no appreciable changes on radioscopy—a small percentage.

The first and commonest sign of mitral stenosis on the X-ray screen is enlargement of the left auricle; this occurred in about 70 per cent as the sole X-ray sign: it is seen best and earliest, in our opinion, in the conventional right oblique position with barium in the œsophagus. In the early case, enlargement is most noticeable with the subject turned through an angle of 60° rather than 45°; but the optimum angle should be chosen. In this position also the pulmonary artery, with perhaps the "conus" of the right ventricle, appears as a prominence on the anterior border of the heart, giving the appearance of great cardiac depth from front to back as compared with the slim-necked normal organ. Master (1942) considers the left oblique position to be of equal value ; and so does Evans (personal communication).

In the right oblique position the course of barium in the œsophagus in the normal is straight

or at most a gentle and slight arc (Fig. 1) ; but in early mitral stenosis, on reaching the upper border of the left auricle, the barium hesitates, *changes its course*, turning backwards before continuing in a curve around the auricle. The bend forming an obtuse angle varies in position, but it is usually high on the posterior cardiac border (Fig. 2, 3, and 4). A wedge of barium may be left at the site of the bend, filling the obtuse angle. Occasionally the convexity may affect not the upper but the middle part only of the auricular curve.

When the left auricular enlargement is but part of a general enlargement, or when this chamber is pushed backwards by a large left ventricle, the barium veers backwards at a high point and runs in a longer curve with its convexity dorsally; there is seldom such a sharp change in direction as in typical mitral stenosis.

An isolated or disproportionate enlargement of the left auricle is almost pathognomonic of mitral stenosis. Apart from a high diaphragm, there are other causes for backward displacement of the œsophagus, for instance, complete heart block (Babey, 1937), pericardial effusion, or patent ductus arteriosus (Donovan *et al.*, 1943). The question as to whether or not the left auricle may enlarge in long-standing auricular fibrillation without mitral stenosis is a matter of opinion; to us it seems probable, but to a limited degree (Babey, 1937; Palmer, 1937). Enlargement of this chamber also occurs in the heart of thyrotoxicosis, but it is more a part of a general enlargement of all chambers.

In the early case in which the right oblique shows a doubtful or borderline enlargement

FIG. 1.—Normal heart. Right oblique position with barium in the œsophagus. Normal left auricular curve.

FIG. 2.—Early mitral stenosis. Right oblique view with barium in the œsophagus. Increased cardiac depth. Barium changes course at a high level with wedging of the barium at the upper border of left auricle as the œsophagus is pushed backwards.

FIG. 3.—Early mitral stenosis. Description as for Fig. 2.

FIG. 4.—Early mitral stenosis. Description as for Fig. 2.

of the left auricle, a straightening of the left border in the anterior view as a separate consideration may assist in coming to the right conclusion on the presence or absence of an early lesion, for the anterior X-ray of mitral stenosis is often also characteristic. The earliest sign is a straightening due to filling-in of the normal concavity of this border by prominence of one or both of the two middle arcs (Fig. 5, 6, 7, and 8).

As some others have done, we deprecate the use of the term " mitralization " for this straightening of the normally concave left border of the heart. By such mixing of the premise and the conclusion in describing an X-ray picture, its real value is diminished. What is seen should be accurately described, and the interpretation for diagnostic purposes should logically follow. Thus straightening of the left border is the observation, and the probable but not the invariable interpretation is mitral stenosis. The upper of the middle arcs is admittedly formed by the pulmonary artery, with or without its left branch. Undue prominence of the upper middle arc (the pulmonary) is almost invariable in established mitral stenosis, but we have only seen it in a small proportion, say 10 per cent, of early cases.

The position as regards the lower middle arc is not so clear. Most cardiologists have believed and taught for years that this arc represents the enlarged conus of the right ventricle which extends forwards and to the left; and that, as the heart rotates to the left, it is thrown

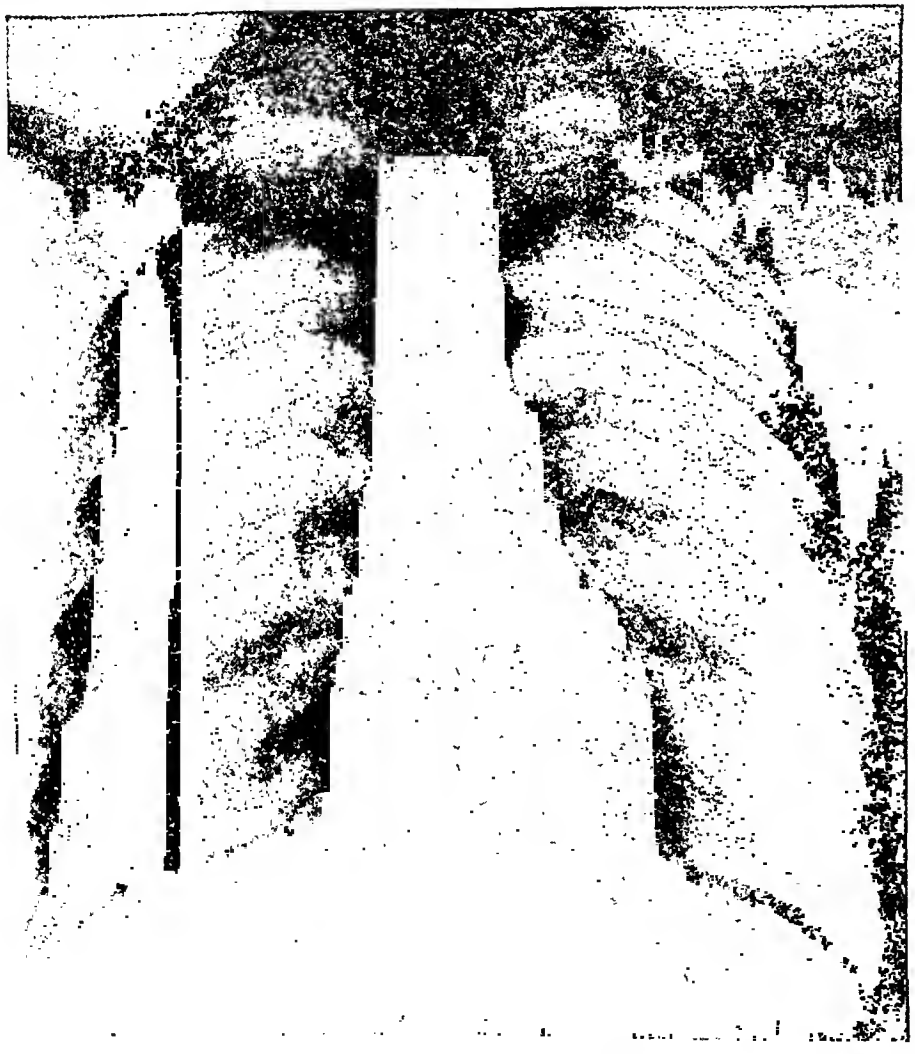

FIG. 5.—Normal heart. Anterior view.

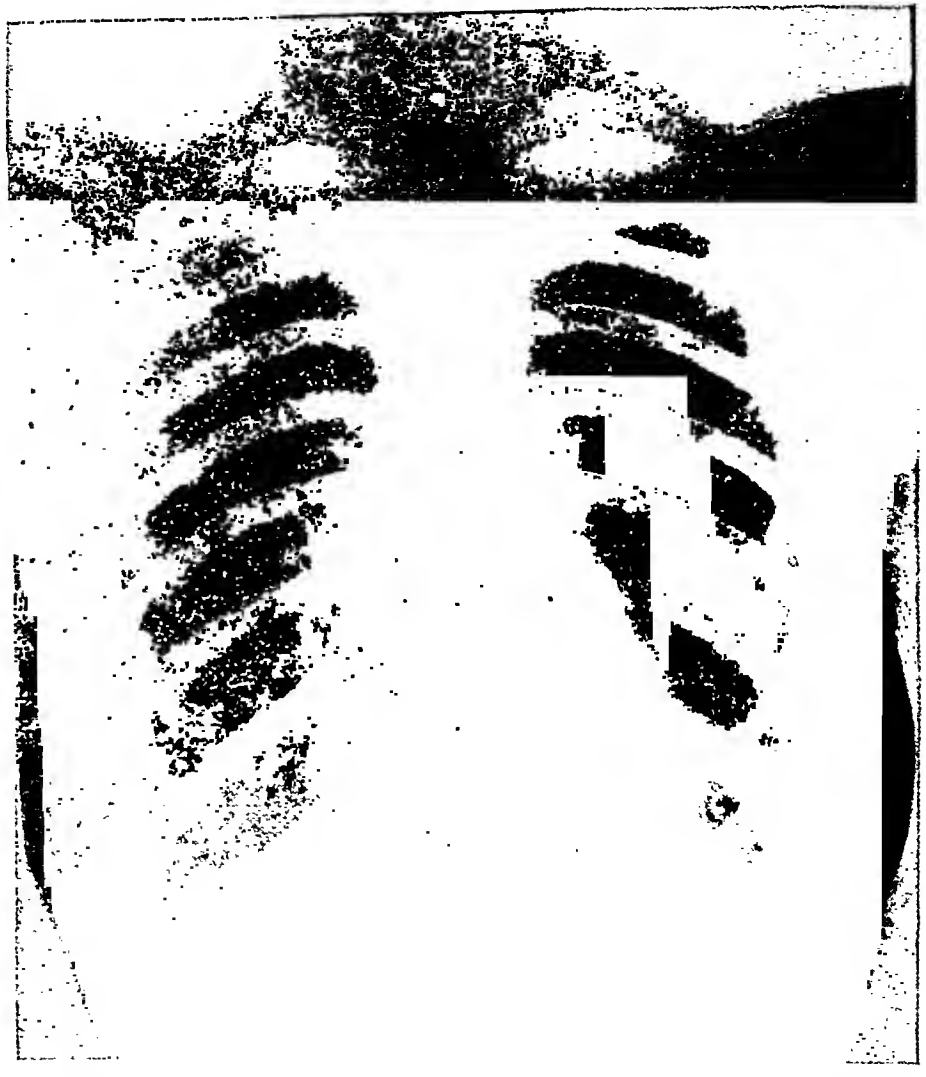

FIG. 6.—Early mitral stenosis. Anterior view. Straightening and lengthening of the left cardiac border by enlargement of the pulmonary artery and "conus."

FIG. 7.—Early mitral stenosis. Anterior view. Straightening and lengthening of the left cardiac border by enlargement of the pulmonary artery and "conus."

FIG. 8.—Early mitral stenosis. Description as for Fig. 7.

into more prominence. This teaching was founded on post-mortem study and found support from Laubry *et al.* (1939), and Roesler (1943). Robb and Steinberg (1939), and Grishman, Sussman, and Steinberg (1944), dispute this belief from their studies with angiocardiograms. They consider that this arc is formed by the left auricular appendage pushed into prominence by the left auricle enlarging to the left, not only to the right; they are convinced that the right ventricular conus never forms part of the cardiac outline as seen by X-ray. On the whole we accept this view.

Since reading this new conception of the identity of the lower middle arc we have taken every opportunity of noting whether while turning the patient to the left (right oblique position) the prominence disappears or persists, and we often find that it persists. If it were the left auricle or its appendage it might disappear with this rotation of the patient (see also Zdansky, 1939). This is not a valid objection to the newer view. The thickness of the ventricular wall is admittedly to be reckoned with. It may be that the undilated appendage sits upon the projecting conus augmenting the prominence. We do not know to what extent the auricular appendage is distended in life; at necropsy it is usually contracted.

Apart from invariable radioscopy which is part of our cardiac ritual, in order to study the anterior outline of the heart in the early stages of mitral valvular disease teleradiograms were taken of 32 men, 17 healthy students, 8 very early but certain mitral stenotics, and 7 men with mitral stenosis and aortic incompetence. This number is admittedly too small for statistical judgment, but they do give some indications of value. These 32 films were taken in 1943, but examined by each of us separately without reference to the clinical findings.

In 21 of the 32 films there was agreement as to the degree of *the hilar shadows*, in 10 of these 21 they were thought to be large or too dense, or both. Valvular lesions were present clinically in 7 of these 10, mitral stenosis with aortic incompetence in 4, mitral stenosis alone in 3. Among the 8 men with early mitral stenosis alone, there were increased hilar shadows in 3, in the other 5 we were not in agreement ; that is in no case of pure mitral stenosis were the hilar shadows considered to be normal by both observers. Among the 7 men with combined valve lesions it was agreed that 4 showed increased markings and that in 1 they were normal ; they was disagreement in 2 cases. The hilar shadows were thought to be normal by both observers in 9 of the 17 normal heart films, to be excessive in 3, and there was disagreement in 5 others. The conclusion may be drawn that the estimation of the degree of hilar markings carries a wide margin of error, yet increase in these shadows does occur rather more frequently in early valvular disease than in normal hearts.

The clinical diagnosis of early mitral stenosis had been made in 8 men ; one of us (J. P.) recognized mitral stenosis in all these films but thought that in 3 it was associated with aortic incompetence; the other (R. H.) considered that 3 of these hearts were within normal limits and also that aortic incompetence was added to the mitral stenosis in 2 others.

The outline of these 8 hearts with early mitral stenosis was traced from the teleradiograms and they were approximated; for comparison, similar tracings of 8 hearts from normal students are shown (Fig. 9). The difference seems to lie first in the straight left border of the group with mitral stenosis, and secondly in the small aortic knuckle in this group, these two points in combination giving an appearance of added length and straightness to the left border of the heart with mitral stenosis. The buttressing, i.e. extension outwards of the right auricle, was possibly a little more prominent in those with mitral stenosis than in those without it, or their right auricular curve may extend a trifle higher. Fig. 6, 7, and 8 show the earliest changes that we consider to be recognizable in mitral stenosis in the anterior view. Fig. 2, 3, and 4 show the earliest changes in the right oblique position. Examples of normal hearts are shown in Fig. 1 and 5 for comparison.

Of the films, 7 in number, of hearts with the combined lesion of mitral stenosis and aortic incompetence, one of us (J. P.) was correct in 5, diagnosed mitral stenosis alone in 1, and considered 1 to be within normal limits. The other (R. H.) thought that 6 showed the combined lesion and that 1 was within normal limits. Both thought one particular film to be that of a normal heart when it was not. The conclusion to be drawn from the films is that, while enlargement of the left auricle in the oblique position is the most certain early sign of mitral stenosis, the anterior film is often abnormal, and nearly always so if a combined valve lesion is present.

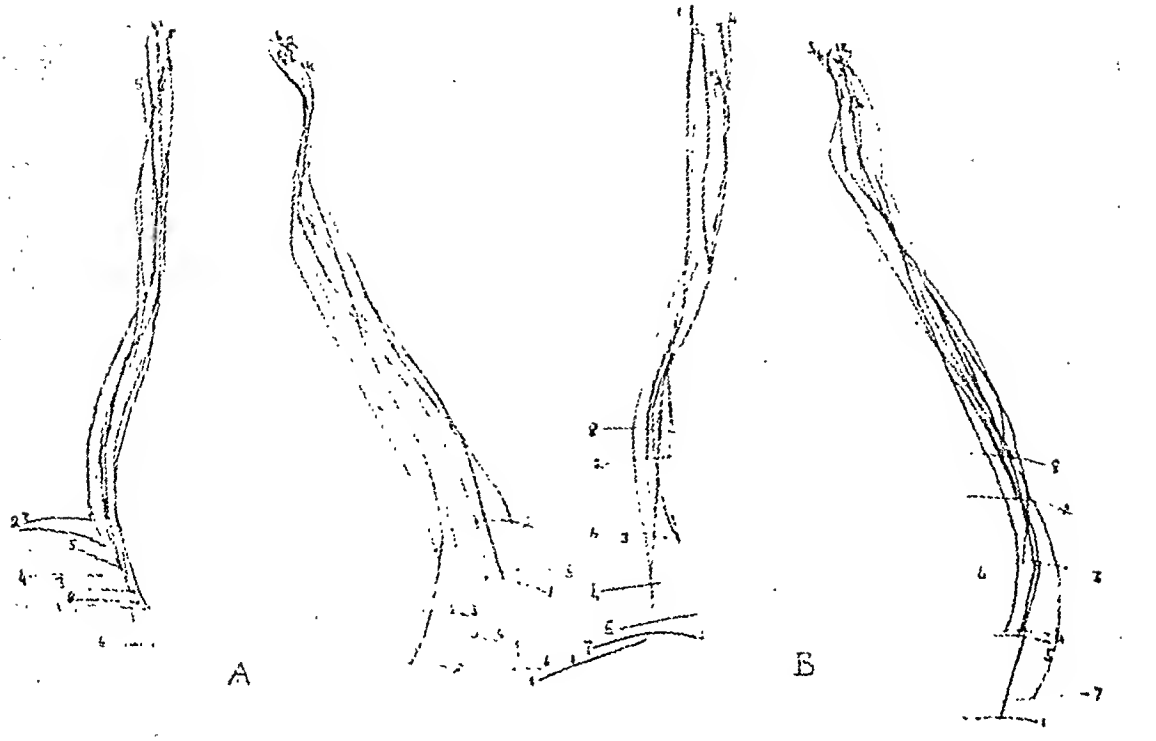

FIG. 9.—Diagram to compare the superimposed outlines of eight normal hearts (A) with those of eight early mitral stenotics; (B) in the anterior view. The difference lies [illegible] and lengthening of the left cardiac border. Buttressing of the right auricle is a less [illegible]

To illustrate those changes that we consider to be the earliest in mitral stenosis we have produced the diagrams shown in Fig. 10 and 11. A normal cardiac outline, taken from a teleradiogram, was used as the normal outline shown by the dotted lines. On to this we have drawn the abnormal outline that we believe to be typical of the early condition. This belief is founded on our experience of radioscopy in the early and symptomless case as seen in recruits.

The question of the differential diagnosis of mitral stenosis from mitral incompetence on radioscopy does not appear easy to decide. Dietlen (1923) considered mitral incompetence to be by far the commonest pure valve lesion seen ; he gave three points of difference from mitral stenosis in early cases : first, the left auricle is enlarged, but not to the same degree as in stenosis ; secondly, the right ventricle is not enlarged except in failure ; thirdly, the left ventricle is enlarged in incompetence, but not in stenosis. Assman (1934) says that there is hypertrophy and dilatation of all the heart chambers except the right auricle in mitral incompetence. Roesler (1943) considers mitral incompetence to be rare, and to cause enlargement of the left ventricle. He draws attention to the pulsations in the large left auricle; in mitral incompetence these are exaggerated and, as they alternate with those of the right lower border, cause a see-saw movement which may be quite distinctive. Zdansky (1939) also speaks of enlargement of the left ventricle, and of the left auricle, though not to the same degree as in mitral stenosis.

We have never felt that this differentiation between mitral stenosis and incompetence can be made radiologically with certainty until kymography is successfully applied to the problem. When, in the presence of a mitral systolic murmur, doubtful or certain enlargement of the left ventricle is seen, it is our practice to listen again for an aortic diastolic murmur. If in mitral incompetence the left ventricle enlarges, and if it is admitted that mitral incompetence develops at a later date into mitral stenosis, the question must arise why the left ventricle is not enlarged in mitral stenosis? Does the left ventricle regress as stenosis is installed ? This is hard to believe.

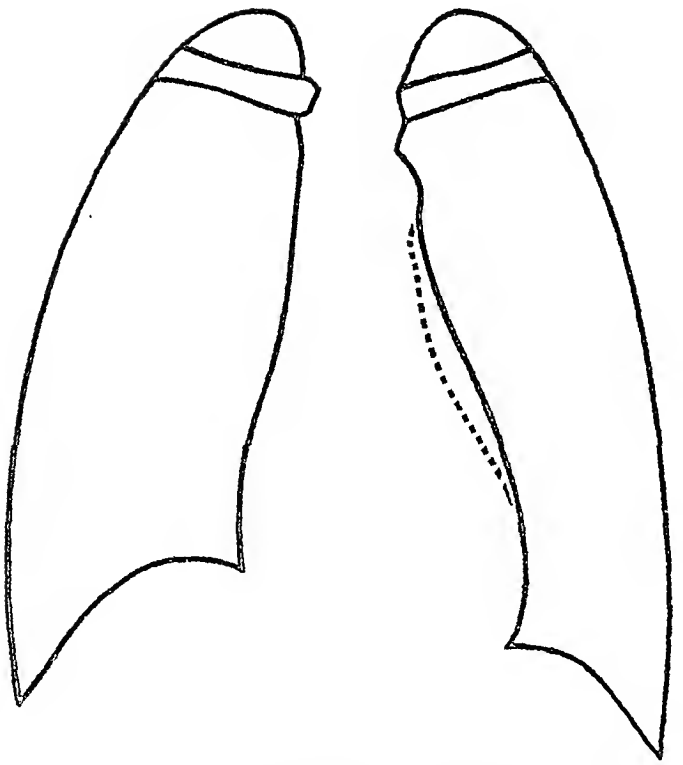

FIG. 10.—Early mitral stenosis. Diagrammatic anterior view. Dotted line denotes normal cardiac outline. Straightening of the left cardiac border by enlargement of the pulmonary artery and "conus," the earliest detectable change in this position.

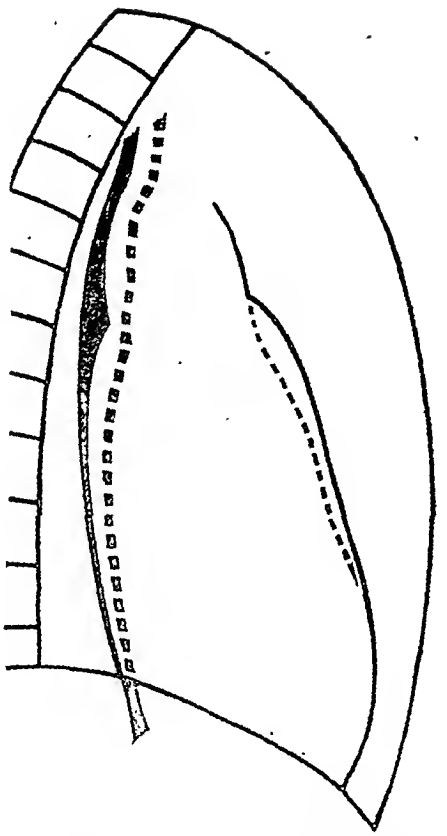

FIG. 11.—Early mitral stenosis. Diagrammatic right oblique view, with barium in the œsophagus. Dotted line indicates the normal heart outline and the normal œsophageal course. Increased cardiac depth, with left auricular enlargement. Anterior and upper cardiac border is fuller and more rounded than the normal.

AORTIC VALVULAR DISEASE

Aortic incompetence

There is remarkable unanimity as to what is the essential early sign of aortic incompetence; it is the aortic diastolic murmur. In early cases this murmur may be inconstant, present only within a limited range of heart rate, or in one position, or indeed on one occasion and not on another. It is usually heard best on the left of the sternum and follows immediately after the second heart sound.

In view of the high incidence rate of aortic diastolic murmurs heard best on the left of the sternum, it is of interest in surface anatomy to note that Sosman and Wosika (1934) have shown that, in disease at least, the aortic valve lies not behind the second right intercostal space, but behind the centre of the sternum, or sometimes to the left of the mid-line. Zdansky (1939) pictures the aortic valve in health to be just below the junction of the superior vena cava and the right auricle, and lying at the left border of the vertebral column in about the centre of the heart shadow at this level. Laubry *et al.* (1939) also indicate that this is the normal site of the aortic valves. Grishman *et al.* (1944) picture the aortic valve as being rather to the left of the mid-line.

Auscultation should be practised with the subject standing, sitting leaning forwards, and lying. As with mitral stenosis, listening to the patient lying down after exertion is useful, for an aortic diastolic murmur may best be heard during the lower ranges of a falling heart rate. The patient should always be asked to stop breathing for a moment at the end of expiration, for this excludes its noise and the respiratory sound which may closely resemble a diastolic murmur. Sometimes an aortic diastolic murmur is audible at the apex and then its early position in diastole, i.e. immediately after the second sound and before the normal time of the third heart sound, aids in its identification (Evans, 1942*a*).

That this murmur is frequently overlooked in recruits is confirmed by the report of Delaney *et al.* (1943) who examined 45,000 air cadets and detected heart disease in 100, 43 of whom showed aortic valvular lesions only; these were men who had been examined several times at medical boards and had been passed fit.

In our series, 202 cases of pure aortic incompetence of rheumatic origin were found. This large figure is significant in that it is a measure of the difficulty experienced by doctors in making this diagnosis. The diastolic murmur may be very difficult to detect unless it is listened for with specific intent, and with ears attuned. Too often an apical systolic murmur, present in 56 per cent of these cases, distracted undue attention upon the mitral valve to the neglect of the aortic and, therefore, to the detriment of the true diagnosis.

That aortic incompetence is frequently missed in life is also shown by a comparison between the clinical and pathological incidence (Tables V and VI). The variation among different authors probably rests on their different criteria of diagnosis in double valvular lesions.

TABLE V

THE VALVES AFFECTED (CLINICAL)

Name	No. of cases	Mitral	Aortic	Both
		Per cent	Per cent	Per cent
Hirschfelder, A. D. (1918)	1781	51	22	20
Willius, F. A. (1927)	160	78	13	9
Wilson, Lingg, and Croxford (1928) ..	328	88	0	11
Findlay, L. (1932)	489	88	0	12
Schlesinger, B. (1938)	738	87	1	11
Ritchie, W. T. (1939)	179	83	1	16
Sosman, M. C. (1939)	738	29	22	49

TABLE VI

THE VALVES AFFECTED (POST-MORTEM)

Name	No. of cases	Mitral	Aortic
		Per cent	Per cent
Coombs, C. F. (1924)	97	100	59
Clawson, B. J., *et al.* (1926)	130	73	63
Glahn, von W. C. (1927)	109	91	58
Findlay, L. (1932)	37	95	59
Bland, White, and Jones (1935)	100	98	71

An aortic diastolic murmur was present in all 202 cases. Dyspnœa was present in 31 (15 per cent compared with 18 per cent in mitral disease). It was recognized during the last war that pure aortic incompetence seldom gave rise to symptoms (Cotton, 1919). Bourne (1940) also found aortic incompetence to be asymptomatic more often than mitral stenosis.

A history of rheumatic fever was obtained in 84 (41 per cent), of chorea alone in 6 (3 per cent), and of both in 8 (4 per cent). The low incidence of aortic incompetence resulting from chorea has often been emphasized (Abt and Levinson, 1916; Strong, 1923; Wallace, 1933; Schwarz and Leader, 1935 ; and Berghoff *et al.*, 1944).

Peripheral vascular signs are absent in early cases ; capillary pulsation, collapsing pulse, and even a large pulse pressure on sphygmomanometry, are to be regarded as confirmatory signs in the developed disease, but render little service in earlier diagnosis.

The X-ray changes in aortic incompetence are confined to the left ventricle and to the aorta. The enlarged left ventricle moves the left border farther out, or the lower and apical portion becomes more rounded, or both these features are present (Fig. 12). In the second oblique position, with the patient turned through an angle of 45°–60°, the rounded left ventricle is in greater contrast with the straight right ventricular arc than in the normal (Fig. 13 and 14).

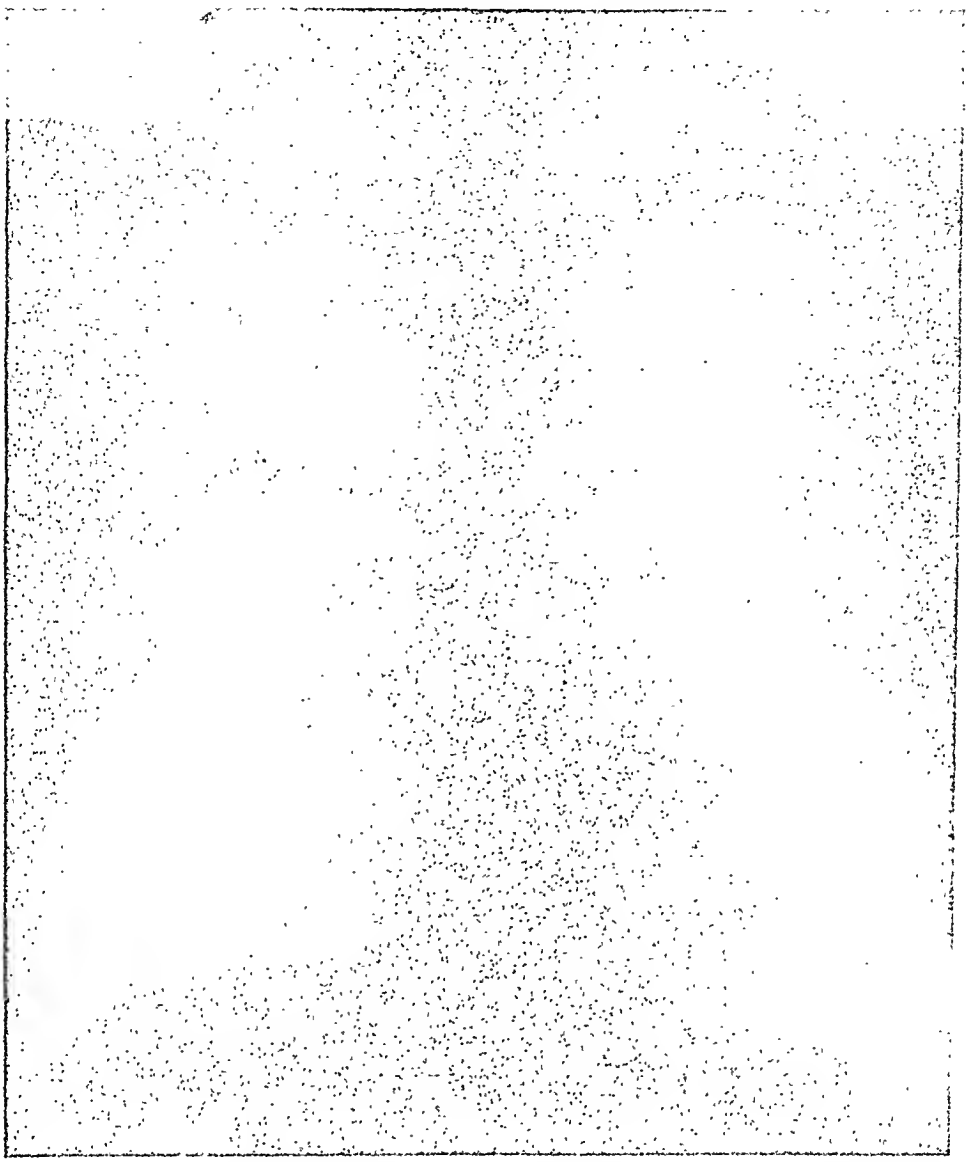

FIG. 12.—Early aortic incompetence. Anterior view. Left ventricle is enlarged to the left and also more rounded than is normal. Ascending aorta is slightly prominent for a young man.

The heart and aorta show excessive pulsation only if the reflux is great enough. A dynamic dilatation of the first part of the aorta is common in rheumatic aortic incompetence and should not easily suggest syphilis.

The diagrams in Fig. 15 and 16 show the changes that we consider to be the early radioscopic signs of aortic incompetence. Upon normal cardiac outlines in the anterior and left oblique positions, shown by the dotted lines, we have drawn that enlargement which our experience of the early and symptomless case, as seen in recruits, has lead us to consider to be the first typical change.

X-ray changes were present in 169 (84 per cent) of these 202 cases, and absent in 33 (16 per cent). The proportion with enlargement is noteworthy when it is remembered that these were early cases and the majority were asymptomatic. Aortic incompetence was strongly suspected in a further 40 cases which were returned as—rheumatic heart disease (probable aortic incompetence). In this group a combination of positive rheumatic history, symptoms, signs, and X-ray findings made the diagnosis likely, but no diastolic murmur was heard with any certainty. One such case was seen in 1942, and again one year later when a diastolic murmur was obvious.

Aortic incompetence of syphilitic origin was the lesion in a further 4 cases.

FIG. 13.—Normal heart. Left oblique view.

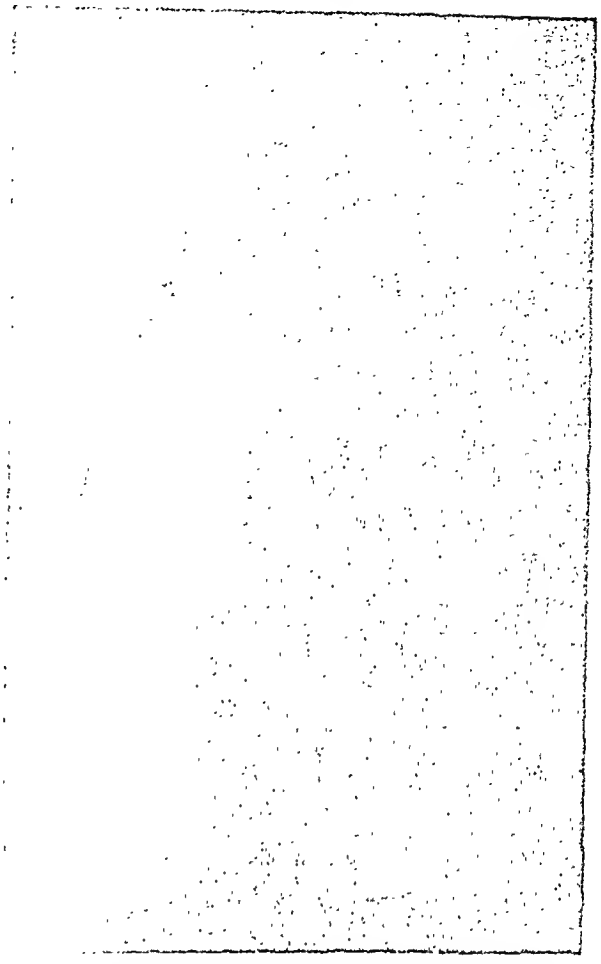

FIG. 14.—Early aortic incompetence. Left oblique view. Rounding and prominence of the left ventricle.

Aortic stenosis

Aortic stenosis alone was present in 14 cases. It is generally considered (Christian, 1931; Clawson *et al.*, 1938 ; Dry and Willius, 1939 ; and Reich, 1945) that aortic stenosis is mostly of rheumatic origin. Gibbs (1935) in his necropsy report found this to be so in 90 per cent under the age of 50, of 27 cases studied.

The diagnosis rests on the finding of an aortic systolic murmur and thrill, with left ventricular enlargement. Whether this diagnosis should be made in the absence of a thrill is debatable—we think it may be made. Reich (1945) recorded its presence in only 27 per cent of 22 cases confirmed post-mortem. A thrill was present in 13 of our 14 cases. The stenotic significance of a loud systolic aortic murmur as the main auscultatory sign in a person suspected of rheumatic heart disease cannot easily be discounted, and with left ventricular enlargement aortic stenosis would become the most likely diagnosis, thrill or no thrill. It is often stated that the aortic second sound is absent in aortic stenosis; but this is not true of early cases. In 13 of our 14 cases the second sound was heard; after the loud murmur, attention may then be directed to hearing the second sound. Analysing the 14 cases: 3 gave a rheumatic history, 6 an apical systolic murmur, and 12 exhibited left ventricular enlargement on radioscopy. Analysis of 13 cases of aortic stenosis with incompetence returned a rheumatic history in 1, dyspnœa in 2, an apical systolic murmur in 7, and X-ray enlargement of the left ventricle in all.

COMBINED VALVULAR LESIONS

Aortic incompetence and mitral stenosis

Aortic incompetence in combination with mitral stenosis was present in 72 cases (10 per

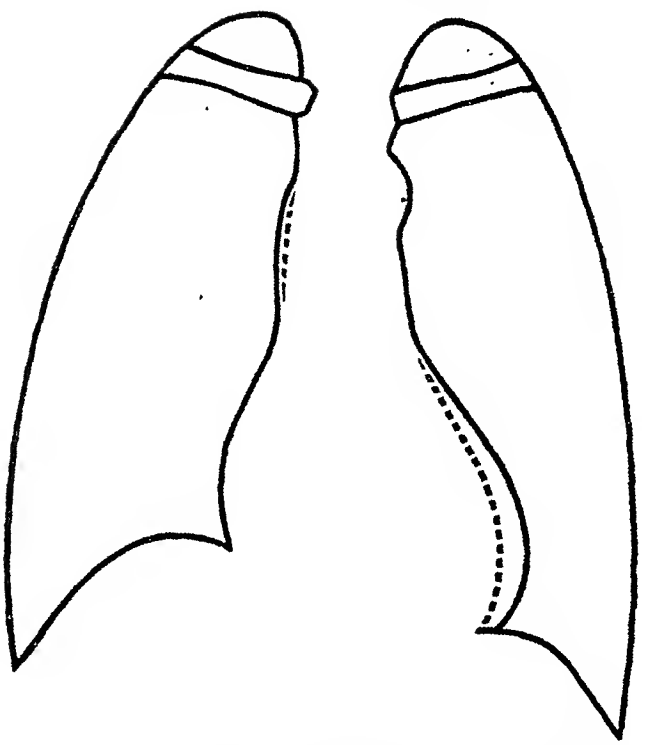

FIG. 15.—Early aortic incompetence. Diagrammatic anterior view. Dotted line is normal heart outline. Left ventricle enlarged to the left, and more rounded than the normal. Ascending aorta prominent.

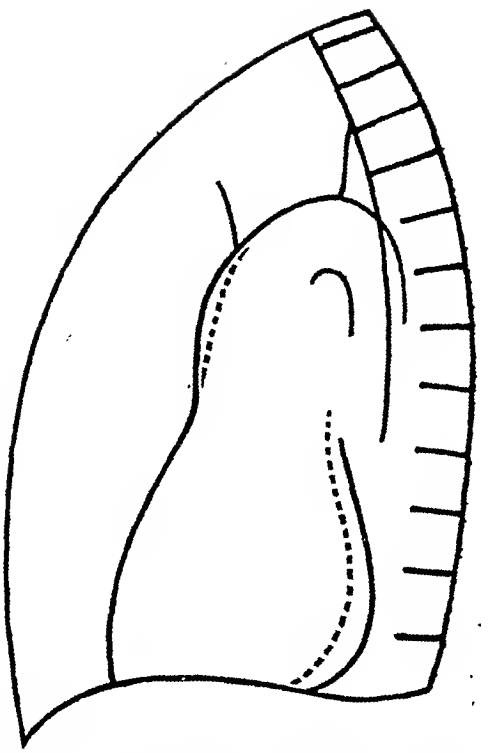

FIG. 16.—Early aortic incompetence. Diagrammatic left oblique view. Dotted line is normal heart outline. Left ventricle enlarged dorsad, and more rounded than the normal. Ascending aorta prominent.

cent) of rheumatic heart disease seen. All these seemed more fully developed than were the single valve lesions and no difficulty was found in their diagnosis.

It must be allowed that 10 per cent of rheumatic cases with this combined lesion does not represent the true figure in all rheumatic heart disease because the grosser cases were graded by the Boards without reference. We believe that this combination is far more frequent than is generally thought, and that the aortic murmur is simply overlooked. Table V shows the clinical frequency as shown by various reported series, and Table VI the post-mortem incidence, the difference between them being obvious.

The findings in our 72 cases are shown in Table VII.

TABLE VII

ANALYSIS OF 72 CASES OF MITRAL STENOSIS WITH AORTIC INCOMPETENCE

Rheumatic history		Dyspnœa	X-ray findings	
Rheumatic fever	23 (32 per cent)	21 (29 per cent)	Left auricle enlarged	53 (74 per cent)
Chorea	6 (8 „)		Left ventricle enlarged	45 (63 „)
Both	3 (4 „)		General enlargement	12 (17 „)
			Normal	4 (6 „)
Total	44 „			

Mitral stenosis, aortic incompetence, and stenosis were present in combination in four cases. A single example of mitral stenosis and aortic stenosis in combination was seen.

Hypertension

The problem of appraising the uppermost limits of the normal blood pressure remains unsolved; for the purpose of admission to the British armed forces a diastolic pressure of 90 must not be exceeded. The question of the significance of a transient hypertension has been much discussed, more in the United States than in this country (Hines, 1940 ; Master, 1943 ; Rogers and Palmer, 1944; and Levy *et al.*, 1944). The conclusions drawn by these

workers is that men showing it, and those with a borderline reading, are more likely to proceed to true hypertension than those without it.

In our 2500 recruits, only 49 (2 per cent) were seen with hypertension, i.e. 6 per cent of all those with heart disease. As noted above, this figure is not a true representation of the frequency of hypertension as compared with rheumatic heart disease. In 45 the systolic and diastolic pressures were both raised, in 2 the systolic only, and in a further 2 the diastolic only. The figure of 160/90 was taken as borderline. The average reading for all these cases was 176/104.

We think that the upper limit of the systolic pressure (after the exclusion of renal disease and coarctation of the aorta) might with safety be placed higher than 160 mm., provided that the diastolic pressure is 90 or below, and that there is no evidence of left ventricular enlargement on radioscopy.

Changes of Pulse Rate

Tachycardia. A simple nervous tachycardia seemed worthy of note in 72 recruits. The pulse ranged between 90 and 130, but usually it fell after rest and as the man became more accustomed to his examiner.

In the United States a persistent heart rate of 100 or over is a cause for rejection (White, 1943). Hoskin (1942) considers that nervous tachycardia should be graded low for service. We believe that a slightly more liberal attitude should be adopted, a rate of 120–130 which tends to fall on resting, in the absence of thyroid disease, may be accepted for full service. We would agree that a persistent rate of 100 should lead to a careful search for a cause other than simple nervousness, such as pyrexia, pulmonary disease, and thyrotoxicosis. Excessive smoking or consumption of alcohol may accelerate the pulse rate.

Bradycardia. This is seldom worthy of note. When the rate is under 50 an attempt to raise the pulse by exercise should be made; when under 40 an electrocardiogram is indicated. Parkinson (1936) has emphasized that simple bradycardia may produce a natural enlargement of the cardiac shadow on X-ray. Two such cases were seen; one because a radiological opinion had been sent to the medical board previously that the heart was enlarged; the other because of the co-existence of a soft systolic murmur.

In 1000 consecutive cases, 31 were referred for irregularity of the pulse.

Extrasystoles	16
Sinus arrhythmia	10
Auricular fibrillation	3
Auricular flutter	1
Tachycardia with ventricular escape	1

In all, 5 cases were seen with auricular fibrillation of undetermined ætiology.

Cardiac enlargement

A difficult problem arose in 25 recruits in whom the heart was enlarged on X-ray, but the cause could not be found. In view of the age group they must be regarded as either congenital or rheumatic. We believe that some of these will eventually develop an aortic diastolic murmur, and this we saw to occur in one case. A further 41 were referred on account of an apparent enlargement from a displaced apex-beat; but actually there was no enlargement, and the displacement was due to scoliosis, which was often more verified on radioscopy than on clinical inspection.

Congenital heart disease

Among the 2500 men seen, 71 had congenital heart disease compared with 609 with rheumatic heart disease.

Pulmonary stenosis	21
Patent ductus arteriosus	10
Atrial septal defect	9
Ventricular septal defect	8
Aortic stenosis	2
Congenital dextrocardia	1
Coarctation of the aorta	1
Right-sided aortic arch	1
Unclassified	18
	71

Finally we would like to support a recent statement by Moir and Shirley Smith (1946) that " the remarkable low incidence of cardiovascular disorders in the Army (less than 7 per 1000 of all sick admitted to hospital) reflects much credit on Recruiting Medical Boards who succeeded in eliminating at the early stage the vast majority of patients with organic cardiovascular disease and to a large extent weeding out those prone to effort syndrome and other neuro-circulatory upsets."

Summary and Conclusions

Medical Boards referred 2500 recruits to one of us for a cardiological opinion before acceptance for military service, and of these, 609 (24 per cent), about a quarter, were judged to have chronic rheumatic valvular disease. The commonest of reasons for reference was the presence of a systolic murmur; others were displacement of the apex-beat, an altered first heart sound, a noticeable third heart sound, arrhythmia, and tachycardia.

Incidental (or functional) murmurs were heard in 259 men (10 per cent). The basis for recognition was their softness and shortness, their variability with posture, respiration, and heart rate. An incidental murmur is seldom loud or long, unless it is of the " late-systolic " variety. A heart found to be of normal shape and size on radioscopy was valuable, and corroborative evidence in deciding that a murmur was incidental. Military as well as medical reasons will decide whether the occasional recruit with a noticeable yet innocent murmur should be accepted for war service.

A split *first-sound* at the apex is a normal variation often mistaken for a presystolic murmur; and slight modifications in the quality of the first sound are negligible. Only in the absence of tachycardia is a loud and abrupt first sound suggestive of mitral stenosis.

Mitral valvular disease was present in 264 men, 32 per cent of all rheumatic cases (609). Pathological evidence is quoted to support the view that mitral incompetence, without stenosis, must occur clinically though it is rare except perhaps in early life. If there is doubt the term mitral valvular disease is convenient.

(*a*) *Mitral stenosis with a presystolic murmur.* 104 cases; all had a loud first sound. In 77 cases enlargement of the left auricle was the characteristic X-ray change: 5 other cases had a loud first sound without a presystolic murmur, and yet X-rays left no doubt that mitral stenosis was present. A mitral diastolic murmur only was heard in 13 other cases.

(*b*) *Mitral stenosis with a systolic murmur.* 60 cases; strong rheumatic history in over half, moderately or very long and loud murmur in all, loud first sound in some and X-ray evidence in 54. In 9 of the 60 cases there was a systolic thrill. In 12 other cases, similar evidence supported in 7 by X-ray enlargement of the heart (though not of the left auricle) seemed to justify a diagnosis of rheumatic mitral incompetence.

(*c*) *Mitral valvular disease* (probable). 68 cases · the history, symptoms, and signs together strongly favoured the diagnosis, but they were not conclusive. In half of them, our X-ray note was " doubtful enlargement of the left auricle." Rejection was always advised.

(*d*) *Mitral stenosis without murmur.* In two cases, one with auricular fibrillation, no abnormal auscultatory signs were found, but the enlargement of the left auricle justified the diagnosis of mitral stenosis.

Aortic valvular disease, without mitral stenosis was present in 229 men.

(*a*) *Aortic incompetence alone.* 202 cases ; all had an aortic diastolic murmur; more than half had also an apical systolic murmur of no great length or intensity. In none was the left auricle enlarged, but in 169 cases (84 per cent) there was enlargement of the left ventricle.

Aortic incompetence alone or in combination with mitral stenosis is far commoner than usually thought. Pathological evidence is quoted in support of our belief. During routine auscultation the possibility of aortic incompetence should always be born in mind, and especially perhaps where there is a systolic murmur at the apex otherwise unexplained.

(*b*) *Aortic stenosis alone.* 14 cases ; 13 had an aortic systolic thrill and yet the aortic second sound was present ; 12 showed enlargement of the left ventricle.

(*c*) *Aortic stenosis and incompetence.* 13 cases ; all had enlargement of the left ventricle.

Combined valvular lesions. Aortic incompetence and mitral stenosis. 72 cases, i.e.

10 per cent of all rheumatic valvular disease seen. Aortic stenosis also was present in 4 other cases.

Radioscopy

This proved to be invaluable in early diagnosis, but electrocardiography was of little value. In no less than 80–90 per cent of these early cases convincing X-ray evidence in support was found.

In the right oblique position the abnormal auricular curve is perhaps seen better on radioscopy than in a film as the course of barium in the œsophagus may be followed; this method also allows the subject to be turned until the optimum position is reached. In the right oblique view the anterior cardiac border in mitral stenosis is prominent and the normal slim neck of the heart becomes filled in and convex.

Left auricular enlargement in mitral stenosis and left ventricular enlargement in aortic incompetence are easily the most important early changes. The enlarged left auricle is confirmed as a sign equal in importance to the presystolic murmur in the diagnosis of mitral stenosis.

Diagrams are shown to illustrate those X-ray changes that our experience in radioscopy of the early and symptomless case has led us to accept as the early signs of mitral stenosis and of aortic incompetence.

A high diaphragm, a trivial scoliosis, or a simple bradycardia simulate (in radiology) an early mitral stenosis or an early aortic incompetence. Either lesion may be concealed by a low diaphragm.

In early mitral stenosis the filling in of the left border combined with a small aortic knuckle, gives a characteristic appearance of added length and straightness to this border. Extension upwards of the right border (buttressing) is unconvincing as an early sign. The density and extent of hilar markings vary so much in health that the occasional increase seen in early mitral stenosis has little value in diagnosis.

In early aortic incompetence the left ventricle enlarges as is shown both by extension outwards of the left lower border and by increased convexity of it. These together are regarded as the earliest signs of left ventricular enlargement. This enlargement is best confirmed in the left oblique position.

Confirmatory teleradiograms were taken in a small series of early valvular disease and in controls, and a few are reproduced in illustration.

We wish to thank Dr. William Evans of the Cardiac Department of the London Hospital for his help in revising this paper; Dr. Alastair Hunter, formerly Chief Assistant in the Cardiac Department, for the normal teleradiograms used as controls; and Dr. John Grimshaw for his valued help with the text.

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PROCEEDINGS OF THE CARDIAC SOCIETY OF GREAT BRITAIN AND IRELAND

The TENTH ANNUAL GENERAL MEETING of the Cardiac Society of Great Britain and Ireland was held at the Physical Chemistry Laboratory, Oxford, on Thursday, April 11, 1946. Chairman F. G. HOBSON.

The Chairman took the Chair at 10.0 a.m.; 64 members and 10 visitors were present.

PRIVATE BUSINESS

1. The minutes of the last meeting having been printed in the Journal (7,210, 1945) were approved and signed.

2. The accounts, audited by East and Brown, were approved: they showed a balance of £17 8*s.* 5*d.* The Council had decided that the ordinary subscription should be collected for the year 1946/47.

3. Maurice Campbell having completed the five years for which he was elected Secretary and five additional years during the war, Shirley Smith was, on the nomination of the Council, elected Secretary, to take office after the conclusion of the present meeting.

4. The following new members were elected:—

Ordinary Members	*Associate Members*
R. Ellis	R. Kempthorne
Evan Jones	Peter Kerley
A. Morgan Jones	D. Lewes
J. D. Olav Kerr	H. E. S. Pearson
W. Phillips	W. Stokes

Eight Associate Members were re-elected for another period of three years.

5. Geoffrey Bourne, London, and J. H. T. Towers, Leeds, were elected members of the Council for the years 1946–50.

6. The following changes in the Rules were carried, *nem. con.*, on the recommendation of the Council:

Rule 1. The Society shall be called the British Cardiac Society.
Rule 4. Insert Corresponding Members.
Rule 6. Ordinary Members shall not exceed 75 (instead of 60).
Rule 9. Associate Members shall not exceed 50 (instead of 30).
. . . not more than 20 instead of 15 shall be allowed in any year.
Rule 15 (New). Corresponding Members may be elected on the nomination of the Council from recognized cardiologists in the British Commonwealth or abroad.

7. The Secretary reported that on the instructions of the Council he had written to the president of the Royal College of Physicians with reference to (i) the appointment of representatives on the Consultant Services Committee, and (ii) the absence of any suggestions for Cardiology in the present list of specialties in a Consultant Service for the Nation. The Society decided to appoint William Evans as their representative on the Consultant Services Committee, and instructed the Secretary to write to the President of the College with regard to the formation of a standing Committee of the College to deal with Cardiology on the same lines as the Committees appointed for other specialties such as Neurology and Dermatology.
8. Correspondence with the Secretary of the Association of Physicians was reported. The possibility of some joint meetings was favoured and the Secretary was instructed to reply accordingly.
9. Williams Evans was again asked to act as Recorder.
10. Cardiac Emergencies was chosen for the main discussion at next year's meeting and the Secretary and Secretary-elect were deputed to divide up the subject and choose opening speakers.

DISCUSSION ON THE TREATMENT OF BACTERIAL ENDOCARDITIS WITH PENICILLIN

R. V. CHRISTIE (*introduced*) described the results of the team of workers who had been treating infective endocarditis with penicillin. Preliminary results had been published in the

Brit. Med. J. (1946, **1**, 881) but he was able to add to the number of cases and to follow them for rather longer.

He concluded that the duration of treatment was most important and the course should be continued for 28 days; that half a million units a day appeared an adequate amount to give; and that heparin should not be added. The occurrence of fever was not a reason for continuing treatment longer. Relapses, if they occurred, were generally in the first 10 days and nearly always in the first 30 days. Relapse after a short course did not seem to prevent later success, but relapse after a long course mattered more. After a relapse the same amount should be given for 6–8 weeks.

The sensitivity of the organism to penicillin did not matter, except that if it was 10 or 16 times more resistent than the standard, the cures were 30 per cent instead of 60 per cent.

The prognosis was better in congenital than in rheumatic heart disease. Severe heart failure was of grave import and 90 per cent died. The state of nutrition was also important and treatment within the first 6 months of onset was favourable.

Heart failure was the main cause of death, and emboli were also important.

G. E. S. WARD described 19 cases of bacterial endocarditis in which a blood culture showed *Streptococcus viridans*, and where 60,000 units of penicillin were injected intramuscularly at three-hourly intervals. Two of the 9 cases given penicillin for 21 days relapsed and had the same dosage for another 28 days. The remaining cases were treated for 28 days and none relapsed. Four of the 19 died, but only one of these could be regarded as having failed to respond to penicillin therapy, for in one cerebral embolism took place on the second day; another died of hæmorrhage from œsophageal veins in hepatic fibrosis; a third died from rupture of an aortic cusp. Of the 15 surviving patients, at least 11 are apparently cured and the other 4 may be. Two have been well for over a year, 5 for almost a year, 4 for nine months and 4 for shorter periods. One had congestive heart failure on two occasions but recovered. Dental extraction appeared to have precipitated the infection in 3 cases, and 9 others had dental sepsis (*Streptococcus viridans*); these 9 had teeth extracted under cover of additional injections of penicillin for 48 hours. Ward emphasized the danger of dental sepsis in rheumatic and congenital heart disease, and the importance of penicillin therapy before dental extraction in such cases. After reviewing the clinical features of the series he said that penicillin sensitivity gave no real clue to the prospect of success or failure, but that the number of colonies grown on culture media seemed to have a bearing on prognosis. Early and prolonged treatment, with adequate dosage of not less than half a million units of penicillin daily for 28 days, was essential; and in the case of a relapse, a further course lasting six weeks should be given.

HENRY COHEN (*introduced*) reported that the Liverpool findings closely paralleled those of other centres. Of 20 unselected consecutive cases (12 m. 8 f.) treated with penicillin, 8 (3 m. 5 f.) patients had died; the remaining 12 had survived for periods ranging from a few weeks to over a year. All three congenital heart cases had responded well. Patients preferred three-hourly intramuscular injection to a continuous intramuscular drip. Cohen spoke of the risks of major emboli, and made reference to a case of aneurysm of the left renal artery which was recognized and successfully treated by nephrectomy, several months after the endocardial infection had subsided. He stressed the importance of appreciating that dangerous sequelæ needing surgical intervention may follow the recovery from infection and the consequent prolongation of life. Another patient had been re-admitted to hospital with rapidly fatal heart failure due to rupture of an aortic cusp recurring long after the infection was overcome, and as the autopsy revealed the endocarditis was healed. Suggestive evidence was forthcoming, though a large scale investigation was necessary for proof, of the value of 100,000 units of penicillin daily for 2 to 3 days following dental extraction or tonsillectomy in a cardiac patient. There must always remain a proportion of cases—probably about 25 per cent who would succumb in spite of adequate penicillin therapy, from congestive heart failure, nephritis, major emboli, ruptured valves and aneurysms, and endocardial reinfection with a penicillin-resistant organism or strain.

GILCHRIST, BOURNE, BRUCE PERRY, and MORGAN JONES also recounted their experiences with a series of cases treated with penicillin.

SHORT COMMUNICATIONS

THE ACTION OF THEOPHYLLINE-ETHYLENE-DIAMINE IN HEART FAILURE

S. HOWARTH (*introduced*), J. MCMICHAEL, and E. P. SHARPEY-SCHAFER found that the theophylline component of theophylline-ethylene-diamine lowered venous pressure, and increased cardiac output in normal hearts. The venous-pressure-lowering action was more persistent than the stimulating action on the heart, the latter being transient and often passing off within half an hour. Striking rises in cardiac output occurred in hypertensive heart failure, but the effects were less prominent in mitral stenosis.

THE HEART IN DEPRESSION OF THE STERNUM

BY WILLIAM EVANS

(Published in full, 1946, 8, 162.)

CHRONIC DISSECTING ANEURYSMS

BY A. MORGAN JONES and F. A. LANGLEY

(Published in full, 1946, 8, 191.)

BERNHEIM'S SYNDROME

TERENCE EAST described three cases in whom the heart failure was of the right ventricular type, although the lesion affected the left ventricle.

The first case was a man of 30 with aortic stenosis. There was the usual congestive failure, but the circulation rate was not greatly slowed. Post-mortem, the aortic valves were calcified, the left ventricle bulged into the right and reduced its capacity, and the lungs were free from engorgement and œdema.

The second case was that of a woman of 47 with aortic stenosis. Post-mortem, the valves were calcified, the lungs were free from œdema and engorgement, the septum bulged into the right ventricle, and there was general anasarca.

The third case was a man with hypertension who had begun to develop signs of right ventricular failure, the lungs remaining clear and the circulation rate not being much slowed.

Casts of the right ventricle in the first two cases were shown illustrating its diminished capacity.

Bernheim's syndrome may be expected in a case with a lesion affecting the left ventricle in whom failure of the right side develops, the circulation time not being unduly prolonged and the lungs remaining relatively clear.

DEMONSTRATION OF INTERATRIAL SHUNTS BY CARDIAC CATHETERIZATION

E. P. SHARPEY-SCHAFER and J. MCMICHAEL said that catheterization allowed the estimation of the oxygen unsaturation of blood in the right ventricle, right auricle, and superior and inferior venæ cavæ. In left to right shunts auricular blood was less unsaturated than caval blood. Estimation of arterial samples indicated right to left shunts. A case was also shown in which other evidence suggested an interatrial shunt but catheterization showed that a shunt was not present.

WOUNDS OF THE HEART

PAUL WOOD drew attention to delayed and recurrent attacks of pericarditis with or without effusion as a sequel to pericardial foreign body.

UNIPOLAR PRÆCORDIAL AND LIMB LEADS

C. W. CURTIS BAIN discussed unipolar chest leads. Standard leads are bipolar, and represent about equally the potentials of the two extremities connected to the galvanometer. With præcordial leads the influence of the remote electrode is very much less than that of the præcordial electrode, since it is so much farther from the heart; but any effect all from this electrode must be regarded as distortion. This applies especially when the potentials

at one point on the præcordium are to be compared with those at another. Wilson in 1932 devised a means of obtaining a remote electrode at almost zero potential, by connecting all three limbs to the galvanometer through a central terminal, and using this as the remote electrode. By this method, according to the Einthoven triangle hypothesis, all forces parallel to the plane of the triangle are cancelled out. There are also forces perpendicular to this plane and these impart a slight negativity to the tracings, but they are probably nearly constant throughout the cardiac cycle, and do not exceed 0·3 mv. For practical purposes these leads (V leads) can be considered to be unipolar. Wilson interposed resistances between each limb and the central terminal, but Goldberger in 1942 showed that they were unnecessary.

When using unipolar leads it is possible to obtain the potentials at any point on the body. Unipolar limb leads, reflecting the potentials at the right arm, left arm, and left leg, are useful in showing the position of the heart. The heart becomes more vertical when there is right-sided hypertrophy or a low diaphragm from emphysema or a long narrow chest. The heart becomes more horizontal when the left ventricle is hypertrophied or when the diaphragm is is high. Six præcordial leads are taken, as standardized by the American Heart Association (1938), extending from the right of the sternum to the mid-axilla. In a normal series the height of R in leads over the right ventricle (V1 and V2) is about half the depth of S; S is absent in leads over the left ventricle (V5 and V6). The transitional point, where R and S are equal, occurs about V3, which lies over the position of the normal septum.

The diagnosis of ventricular hypertrophy is based on the relative time taken by the impulse to spread through each ventricle. It is, therefore, unaffected by the position of the heart. In left ventricular hypertrophy R becomes small and S deep in leads V1 and V2; the voltage of the complexes usually increases; the transitional point swings to the left; in advanced cases T is inverted in V5 and V6. In right ventricular hypertrophy a Q wave appears followed by a large R in V1 and V2; there is no S. In V5 and V6, S waves are seen, but there is no abrupt transitional point.

When left-sided weakness is followed by right-sided hypertrophy, as in many cases of advanced hypertension, standard leads usually fail to show axis deviation, since the vertical twist of the heart caused by the right-sided hypertrophy cancels out the left axis deviation. Chest leads, however, continue to register the lengthened time taken by the impulse to pass through the thickened left ventricle. At the same time unipolar limb leads will show that the heart is vertical.

Chest leads in bundle branch block have the same general characteristics as in hypertrophy, but the QRS is widened. In left branch block a deep S follows a diminutive R in V1 and V2; in V5 and V6 a broad R occurs, and there is no S. In right branch block a broad R, sometimes preceded by a Q, is seen in V1 and V2, and a slender early R followed by a broad S in V5 and V6. Concordant and homophasic curves are shown to be due only to unusual positions of the heart. It is nearly always possible to determine the side of the lesion.

Anterior infarcts can be divided into antero-septal and antero-lateral types, according to whether the changes are more pronounced towards the right or left. Antero-septal infarcts often do not cause characteristic changes in lead I: small ones may only show inversion of T in V1, V2, and V3, and so would be missed if lead IV only were taken. Large anterior infarcts have deep Q waves and inversion of T in all the chest leads. Involvement of the septum can sometimes be diagnosed. Left branch block obscures the changes of infarction, since the left ventricle receives the impulse late. But this does not apply to right branch block, and the characteristic changes of branch block and the anterior infarct can both be seen clearly.

Heart Failure of Unknown Aetiology in Africans

D. Evan Bedford and G. L. S. Konstam (*introduced*) described a series of 40 cases of unexplained heart failure in African troops, mostly from West Africa, serving in the Middle East. Their ages were usually between 20 and 30, and all but two were under 40. They were admitted to hospital either with severe left heart failure or with combined pulmonary and systemic congestion and ascites. The history was of increasing dyspnœa for a few weeks or months, and sometimes of attacks of nocturnal dyspnœa with hæmoptysis. The main clinical

findings were normal rhythm with a very small rapid pulse, and often extrasystoles. Alternation was the rule. The heart was grossly enlarged to the left, and the sounds distant with a triple rhythm at the apex; systolic murmurs were common and the pulmonary second sound was much accentuated. The blood pressure was often low, below 120 mm. systolic, but sometimes slightly raised to 140 to 160 systolic. The diastolic was relatively high, often 100 mm. or just over. X-rays showed gross general enlargement of the heart with a prominent pulmonary artery and conus, and in half the cases the aorta was unduly small.

The Kahn was positive in about half, but this was common in African patients and ascribed to previous infection with yaws. The urine was usually normal and there was no evidence of nephritis. Blood examination rarely showed any anæmia and sickling was excluded, but eosinophilia was sometimes present. Ankylostomiasis and other parasitic infestations were common. There was no evidence of avitaminosis, no peripheral neuritis, and no malnutrition. The diet was adequate and far better than they were accustomed to at home.

There was no response whatever to thiamin given in adequate doses, both intravenously and by mouth. The response to digitalis and mersalyl was moderate. Some improved and became free from congestive heart failure, though they could do little; in these the heart diminished in size, though remaining considerably enlarged. Seventeen patients had died in hospital and necropsies were done in all these.

The hearts showed gross enlargement involving all cavities, and due more to dilatation than hypertrophy, though the weight was increased. There was no valvular disease, except in two cases with old mitral endocarditis and thickening. The coronary arteries were healthy in all. In three cases there was marked hypoplasia of the aorta, but the size of the aorta had not been specially noted in the earlier necropsies. In some cases there was an obvious and extensive subendocardial fibrosis, with fibrous areas resembling shallow infarcts in the ventricles, adherent to which was organized antemortem clots. Histological examination was still in progress, but some sections examined had shown extensive subendocardial necrosis and fibrosis without appreciable inflammatory reaction.

The ætiology was briefly discussed in relation to hypoplasia of the aorta, primary myocardial failure of French authors, "isolated myocarditis," hypertension, nutritional deficiencies, and tropical diseases. The clinical and pathological findings corresponded to cases described in America of recent years under the heading of "isolated myocarditis" or Fiedler's myocarditis, and especially to those described by Smith and Furth in 1943. The possibility of heart failure being the end result of previous nutritional deficiency had to be considered, as had a constitutional factor associated with aortic hypoplasia.

Thoraco-Lumbar Sympathectomy and Hypertension

W. T. Cooke and J. A. Barclay (*introduced*) presented the results of thoraco-lumbar sympathectomy (performed by W. H. Sweet) in 23 cases with hypertension. According to the criteria adopted by Keats, Wagener, and Barker, ten were Grade 4, six Grade 3, and the remaining seven Grade 2. Encouraging results were noted in Grades 3 and 4, twelve to forty months after operation. Two cases died before the completion of the second stage and one twelve months later. The remainder showed marked symptomatic improvement, resolution of eye changes, and a return to normal blood pressure in three. Studies of renal function in 5 patients, before and after operation, and 4 further patients before operation, showed a marked fall in Tm. The ratio of blood flow to Tm, however, was increased in varying degree in all cases except one in whom renal biopsy showed marked arteriosclerotic changes. Operation did not affect the ratio. The findings supported the observations of others, that the renal changes were probably not a primary factor in the genesis of essential and malignant hypertension.

Dextrocardia from Eventration of the Diaphragm

J. K. Rennie described a woman who had been suffering from bronchitis for three weeks. Dullness had been noted at the left base and was ascribed to fluid. She was a frail woman of 69 who had never suffered from any serious illness except she had a gastro-enterostomy performed for suspected duodenal ulcer 22 years before. The chest was very narrow, with

much kyphosis. On the right side in the fifth interspace a pulsation was apparent four inches from the midsternal line, which on palpation was found to be undoubtedly the apex beat. There was dullness half-way up the left back with absent respiratory murmur. The cardiogram proved to be normal. X-ray revealed a typical Petit's eventration of the left diaphragm with pronounced displacement of the heart to the right (plates shown revealing characteristic deformity). Displacement of the heart to the right is, of course, a constant finding in eventration of the left diaphragm but this is generally remarkably small in extent, even in middle-aged patients. This case shows how dextrocardia may be simulated, especially in the elderly with the chest changes described for this patient.

Acute Pericarditis in Still's Disease

Bernard Schlesinger mentioned that an adherent pericardium was not an uncommon finding at autopsy in the earliest accounts of this disease, but it was remarkable how this had rarely given rise to symptoms or signs during life, and for this reason it had never been suspected. He then described four cases that began with high fever, great distress, and evidence of acute pericarditis. This was subsequently followed by glandular enlargement, splenomegaly, a rash, and general rheumatoid involvement of the joints. A high leucocytosis was one of the features. Pericarditis thus appeared to be a definite and important part of the clinical picture of rheumatoid arthritis in childhood. The sequence of events favoured some specific infection, as yet unidentified, as the cause of rheumatoid arthritis. Finally he concluded that the separation of rheumatic fever and rheumatoid arthritis into two watertight compartments might not be justified and should receive further consideration.

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MADE AND PRINTED IN GREAT BRITAIN BY
D. R. HILLMAN & SONS
FROME